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DRUG-INDUCED HÆMOLYTIC ANÆMIA AND FAVISM.

By A. D. McCUTCHEON, M.D., M.R.A.C.P.[1]

From the Baker Medical Research Institute, Melbourne.

THE ever-increasing range and effectiveness of medical drugs have been paralleled by a similar increase in unpleasant side effects. A notable example is the occurrence of acute hæmolytic anæmia in certain patients treated with the anti-malarial drug primaquine, and study of this drug sensitivity has shed new light on the old problem of hæmolysis.

Beutler (1959), in a recent review of this subject, described the intrinsic enzyme defects in primaquine-sensitive erythrocytes, and indicated that these cells are also uniquely sensitive to a number of other drugs including sulphanilamide, acetanilid, phenylhydrazine, phenacetin, sulphacetamide and thiazolsulfone.

In the present paper, five cases of drug-induced hæmolytic anæmia are recorded, four of which were due to ingestion of phenacetin. It was decided to investigate these patients to see whether they had the same class of intrinsic enzyme defect as patients with primaquine-sensitive erythrocytes.

An Italian boy with a past history suggestive of favism was also available for study. Favism may be defined as an acute hæmolytic anæmia following ingestion of the ordinary broad bean (*Vicia faba*). It has a familial tendency and a racial distribution, especially in the Mediterranean littoral.

Historical Survey.

Dern and his associates (1954) first established that sensitivity to primaquine in Negroes was due to an intrinsic abnormality of the erythrocytes. They labelled erythrocytes from primaquine-sensitive individuals with radiochromium (^{51}Cr) and transfused them into non-sensitive recipients, who were subsequently given primaquine. Only the labelled erythrocytes were lysed, not the recipients' own cells.

Further studies by Beutler *et alii* (1954*a*, 1954*b*) showed that the hæmolytic anæmia was frequently associated with the formation of refractile particles (Heinz bodies) in the erythrocytes, and that only the older erythrocytes were destroyed. Reticulocytes were resistant to destruction by primaquine and also resistant to Heinz body formation.

Beutler *et alii* (1955*a*) published their Heinz body incubation test, in which blood was incubated with acetyl phenyl hydrazine or hydroxylamine, to produce one large, well-rounded Heinz body and frequently one or two smaller ones in the majority of normal erythrocytes (Figure I).[1]

[1] E. H. Flack Research Fellow, 1959.

[1] For Figures I and II see art-paper supplement.

Of erythrocytes sensitive to primaquine, more than 45% contained five or more Heinz bodies.

While studying various enzyme systems in the erythrocytes, Beutler *et alii* (1955*b*) found that erythrocytes of primaquine-sensitive subjects were deficient in reduced glutathione (GSH). Glutathione is a tripeptide containing a sulphydryl group, and it is a reducing substance capable of protecting cells to some extent from the effects of radiation and from poisoning by arsenic. These workers also showed that inhibition of sulphydryl compounds in normal erythrocytes caused them to behave like primaquine-sensitive cells with respect to Heinz body formation. Hence it was postulated that reduced glutathione (GSH) acts by protecting the cell from the action of injurious substances which oxidize hæmoglobin or stroma, and which thereby produce Heinz bodies.

Carson *et alii* (1956) demonstrated that primaquine-sensitive cells were deficient in the enzyme glucose-6-phosphate dehydrogenase (G6PD). Normal erythrocytes maintain GSH in a reduced state by means of an enzyme, glutathione reductase (G reductase), which itself is dependent upon the presence of reduced tri-phosphopyridine nucleotide (TPNH). TPNH is generated primarily from the oxidation of glucose-6-phosphate by the enzyme glucose-6-phosphate dehydrogenase (G6PD)—for example:

(1) Glucose-6-phosphate + TPN $\overset{\text{G6PD}}{\rightleftharpoons}$ 6 phosphogluconate + TPNH + H^+.

(2) GSSG + TPNH + H^+ $\overset{\text{G. reductase}}{\rightleftharpoons}$ 2 GSH + TPN

(GSSG = oxidized glutathione, TPN = triphosphopyridine nucleotide).

It follows, therefore, that cells deficient in G6PD would be unable to maintain glutathione in a reduced state because of a secondary inability to produce TPNH.

Beutler (1957) described a glutathione stability test, in which blood was incubated for two hours with the same sorts of substances that produce Heinz bodies. In normal individuals there was little or no fall in erythrocyte GSH concentration after incubation; but in primaquine-sensitive individuals the GSH level fell almost to zero.

As a result of these investigations, three tests are available for the detection of a specific enzyme defect in cases of drug-induced hæmolytic anæmia: (i) the Heinz body incubation test; (ii) the glutathione stability test; (iii) direct measurement of G6PD activity in erythrocytes.

Application of these tests in the last two years has shown that the enzyme deficiency in primaquine-sensitive erythrocytes is also demonstrable in the erythrocytes of patients with favism (Szeinberg *et alii*, 1958; Zinkham *et alii*, 1958), of children with hæmolytic anæmia following ingestion of naphthalene (Dawson *et alii*, 1958; Zinkham and Childs, 1957), of Sephardic Jews who develop hæmolytic anæmia after sulphonamide therapy (Szeinberg *et alii*, 1958), and of Negroes with hæmolytic anæmia induced by nitrofurantoin (Kimbro *et alii*, 1957).

Other enzyme abnormalities have been demonstrated in primaquine-sensitive erythrocytes, notably an increase in aldolase and in glutathione reductase (Schrier *et alii*, 1957; Schrier *et alii*, 1959).

Materials and Methods.

The following subjects were studied: five patients with drug-induced hæmolytic anæmia; one boy of Italian origin, thought to have had favism three years previously; the boy's parents; and one patient with acquired hæmolytic anæmia. (See case reports.)

Heinz body incubation tests and GSH stability tests were performed as described by Beutler *et alii* (1955*a*) and by Beutler (1957), except that hydroxylamine hydrochloride was used insthead of acetyl phenylhydrazine, in amounts of 4 mg. per 100 ml. in glucose phosphate buffer for the Heinz body test and of 1 mg. in 1 ml. of blood for the GSH stability test.

G6PD activity was measured in the erythrocytes of the boy with favism, and of the boy's father by Mr. Ian Parsons, at the Peter MacCallum Institute, and I am indebted to him for these results. The method used is described by Zinkham *et alii* (1958).

Results.

Heinz Body Incubation Test.

Forty normal individuals were tested, the common staining reaction being that seen in Figure I. In two normal subjects 34% of erythrocytes had five or more Heinz bodies per cell. This compares with the range of 0 to 28% in normal blood given by Beutler *et alii* (1955).

Four of the five patients with drug-induced hæmolytic anæmia (one was not tested) and the patient with acquired hæmolytic anæmia fell within the normal range (Table I). In contrast, the boy with favism showed 50% of erythrocytes with more than five Heinz bodies (Figure II), and these bodies were smaller than those seen in normal blood. This corresponds with the picture seen in primaquine-sensitive erythrocytes. The boy's parents gave normal results to Heinz body incubation tests.

TABLE I.
Heinz Bodies in Erythrocytes.

Case Number.	Diagnosis.	Percentage of Erythrocytes with More than Five Heinz Bodies.
—	Normal range.	0 to 34
I	Drug-induced anæmia.	6
II	Drug-induced anæmia.	6
III	Drug-induced anæmia.	10
IV	Drug-induced anæmia.	(Not examined)
V	Drug-induced anæmia.	5
VI	Acquired hæmolytic anæmia.	15
VII	Favism.	50
VIII. (Father of subject in Case VII)	—	Nil
IX. (Mother of subject in Case VII)	—	16

GSH Stability Test.

The average concentration of reduced glutathione in the erythrocytes of 64 normal people was 70 mg. per 100 ml. of erythrocytes, with a range of 42 to 93 mg. per 100 ml. and a standard deviation of 11·3.

After incubation with hydroxylamine, the average concentration of GSH had fallen to 46 mg. per 100 ml. of erythrooytes with a range of 30 to 77 mg. per 100 ml. and a standard deviation of 10·3 (Table II, Figure III). This is a greater fall than Beutler *et alii* (1957) found using the different drug acetyl phenylhydrazine.

The results from the patients with drug-induced hæmolytic anæmia were all within the normal range, but the boy with favism showed an abnormal drop in GSH (Table II, Figure III)—again similar to that seen in primaquine-sensitive erythrocytes.

G6PD Activity.

The normal range for the method used is 150 to 210 units per 100 ml. of blood. G6PD activity in the boy with favism was only 6 units per 100 ml. of blood, and in his father it was 180 units per 100 ml. of blood.

Reports of Cases.

CASE I.—A woman, aged 61 years, was admitted to hospital in September, 1958, with a hæmoglobin value of 7 grammes per 100 ml. and a reticulocyte count of 34%. A supravital preparation showed 50% of erythrocytes to contain Heinz bodies. The serum bilirubin content was 1·6 mg. per 100 ml., and the serum also contained methæmalbumin. The response to a Coombs test was negative. In the blood film, erythrocytes showed marked anisocytosis and polychromasia, with numerous "burr", fragmented, and stippled cells, Howell-Jolly bodies and Pappenheim's bodies. The patient had been taking tablets containing a total of 30 grains of phenacetin per day for several weeks.

CASE II.—A woman, aged 82 years, was admitted to hospital with a partial bowel obstruction. Two weeks later her hæmoglobin value was found to be 8·8 grammes per 100 ml. and her reticulocyte count 3%, and a blood film was suggestive of drug-induced anæmia. A supravital preparation showed many cells containing Heinz bodies. The only drug which could be implicated was sulphadimidine, given in routine dosage for a urinary tract infection. When the drug was stopped, the hæmoglobin value returned towards normal and erythrocyte abnormalities disappeared.

CASE III.—A woman, aged 48 years, had been taking tablets containing a total of 20 grains of phenacetin daily for nine weeks. The hæmoglobin value was 12 grammes per 100 ml., the reticulocyte count was 6%, and the blood film had the appearance of drug-induced hæmolytic anæmia.

TABLE II.

Case Number.	Diagnosis.	Milligrammes of G.S.H. per 100 Millilitres of Erythrocytes.	
		Before Incubation.	After Incubation.
—	Normal group.	Average, 70	Average, 46
I	Drug-induced anæmia.	73	58
II	Drug-induced anæmia.	71	47
III	Drug-induced anæmia.	76	32
IV	Drug-induced anæmia.	80	44
V	Drug-induced anæmia.	78	50
VI	Acquired hæmolytic anæmia.	76	39
VII	Favism.	48	11
VIII. (Father of subject in Case VII)	——	69	49
IX. (Mother of subject in Case VII)	——	85	55

Range before incubation, 42 to 93; S.D., 11·3.
Range after incubation, 30 to 77; S.D., 10·3.

CASE IV.—A woman, aged 71 years, was admitted to hospital with myocardial infarction. Her hæmoglobin value was then 16·7 grammes per 100 ml. Five weeks later the hæmoglobin value was 11 grammes per 100 ml., and the blood film suggested hæmolytic anæmia, with anisocytosis, polychromasia and many small irregular cells. The reticulocyte count was 8%. She had been given many drugs, including compound tablets of codeine (B.P.), for facial pain.

CASE V.—A woman, aged 63 years, had been previously treated for barbiturate and alcohol addiction. Just before her admission to hospital, she had taken an unspecified number of "Bromural" tablets (containing monobromisovaleryl-carbamide) and 20 "Veganin" tablets (containing a total of 80 grains of phenacetin). On her admission, the hæmoglobin value was 11 grammes per 100 ml., and on succeeding days it fell to 8·2, 7·0 and 5·0 grammes per 100 ml. respectively. The leucocytes numbered 32,000 per cubic millilitre, the reticulocyte count was 7%, and 90% of erythrocytes contained Heinz bodies. Methæmoglobin was detected spectroscopically.

CASE VI.—A man, aged 66 years, had acquired hæmolytic anæmia. He gave positive results to the Coombs test and the Wassermann test and had a reticulocyte count of 39%. L.E. cells were found.

CASE VII.—This patient was an Italian boy, aged five years. When aged 27 months he had presented with diarrhœa, vomiting, pallor, slight icterus and a hæmoglobin value of 4·2 grammes per 100 ml. A blood film confirmed the diagnosis of hæmolytic anæmia. The reticulocyte count was 12%. The spleen was not palpable. There was a history of eating broad beans 24 to 28 hours before his admission to hospital. He received a blood transfusion and has remained well since then.

Discussion.

Three tests are now available for studying cases of drug-induced hæmolytic anæmia, which give some indication of the presence or absence of the erythrocyte enzyme glucose-6-phosphate dehydrogenase. As patients with deficiency of this enzyme may be sensitive to a number of commonly used drugs, it is important to identify the defect in order that subsequent attacks of hæmolytic anæmia may be prevented.

The Heinz body incubation test is simple to perform, and there is usually a clear-cut difference between the normal person and the person with deficiency of G6PD. However, results may be influenced by variations in the hæmatocrit and oxygenation of the venous sample (Beutler, 1957) and equivocal results may be obtained in other hæmolytic states, especially congenital spherocytic anæmia and acquired hæmolytic anæmia.

The glutathione stability test is more complex and probably more specific, although occasional discrepancies between results of this test and estimation of G6PD activity have been reported (Beutler, 1959).

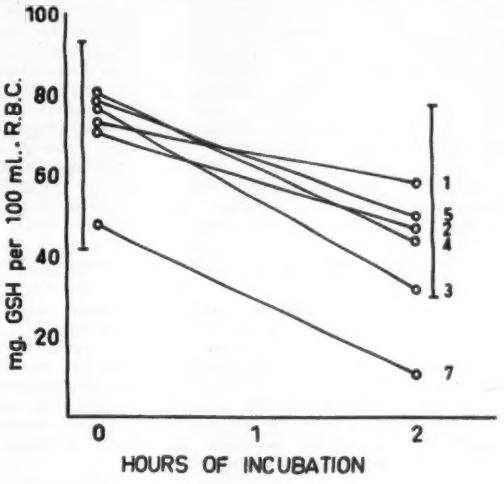

FIGURE III.

Reduced glutathione (GSH) concentrations in the erythrocytes of five patients with a drug-induced hæmolytic anæmia (Cases I to V), and of one patient with favism (Case VII), before and after incubation with hydroxylamine. The normal range is shown by the two vertical lines.

Reduced glutathione may protect erythrocytes from drugs which oxidize stroma; but the exact relation between GSH depletion in the erythrocyte and hæmolysis is not clear, and may even be fortuitous.

The erythrocyte stroma consists of lipoprotein, and Beutler (1959) has suggested that it is the associated deficiency of TPNH which may lead to cell damage by interfering with lipid synthesis.

Evidence to support this has been provided by James *et alii* (1959), who have demonstrated "the ability of the cellular components of blood to synthesize a wide variety of fatty acids", and by Langdon (1957), who believes that the rate of fatty-acid synthesis may be highly dependent upon the availability of TPNH.

These two tests therefore act as indicators of the ability of erythrocytes to resist damage done by various agents, and are very good screening tests for detecting G6PD deficiency.

The positive response to the Heinz body incubation test and the abnormal result of the glutathione stability test in an Italian boy with a past history suggestive of favism provided strong evidence of deficiency of G6PD, and this was confirmed by direct measurement of G6PD activity.

With the continued influx of migrants from the Mediterranean region, many more of these cases will be seen. Such patients should be warned against the use of sulphonamide drugs and analgesics containing phenacetin, as well as against eating broad beans.

The fact that the results of Heinz body incubation tests and GSH stability tests were normal in the group of drug-induced hæmolytic anæmias studied here strongly suggests that there was no lack of the enzyme G6PD, despite lack of direct measurement of G6PD activity. These patients were all females of Western European type, in which the enzyme defect is rare, and phenacetin was responsible for the anæmia in four out of five cases.

However, Houston and Barlow (1959) have recently described a case of acute hæmolytic anæmia with hæmoglobinuria produced by 0·6 gramme of phenacetin, in which the Heinz body test and GSH stability test both gave positive results, indicating deficiency of erythrocyte G6PD. They differentiate this acute type of illness from hæmolysis occurring after prolonged phenacetin therapy, in which "intracellular methæmoglobinæmia appears first". However, it is very doubtful whether theses two groups of phenacetin-induced hæmolytic anæmias can be so easily differentiated (except by tests for G6PD deficiency), for the following reasons: (i) The commonest pigment change produced by phenacetin is sulphæmoglobin, not methæmoglobin, which is rare (Eaton, 1959). (ii) Anæmia is not a feature of the cases in which pigment changes occur (Brandenburg and Smith, 1951). (iii) The development of hæmolytic anæmia after ingestion of phenacetin does not appear to be proportional to the amount of phenacetin taken, or to the degree of either sulphæmoglobinæmia or methæmoglobinæmia. Some other mechanism must be sought to explain the occurrence of anæmia in these cases, including Case II, in which no phenacetin was given.

MacGibbon et alii (1960), in a very recent paper, describe two cases of hæmolytic anæmia with oliguria in which an auto-antibody acting on the patient's erythrocytes in the presence of the drug was demonstrated. In one case the anæmia followed ingestion of small amounts of phenacetin, and in the other, treatment with *p*-aminosalicylic acid. Such a mechanism may be responsible for most cases of drug-induced hæmolytic anæmia in which erythrocyte G6PD deficiency has been excluded.

Summary.

1. The application and significance of tests for the detection of deficiency of the enzyme glucose-6-phosphate dehydrogenase in drug-induced hæmolytic anæmias is discussed.

2. A case of favism is presented, in which there occurred a positive response to the Heinz body incubation test, an abnormal response to the glutathione stability test, and a deficiency of G6PD activity.

3. Five cases of drug-induced hæmolytic anæmia in Western European type people, found to give normal results to Heinz body and glutathione stability tests, are presented. The mechanism of anæmia in these cases is discussed.

4. With the continued influx of migrants from the Mediterranean region, more cases of favism and drug-induced hæmolytic anæmia due to deficiency of glucose-6-phosphate dehydrogenase will be seen. Diagnosis of the specific defect is important in preventing further attacks of hæmolysis.

Acknowledgements.

My thanks are due to Dr. F. Hird, Biochemistry Department, University of Melbourne, for supplying a satisfactory sample of reduced glutathione; to Dr. G. C. de Gruchy, who allowed me to investigate Case III; to Dr. M. P. Shoobridge for Case V; and to Dr. M. Berah and Dr. W. F. Breidahl for access to the Italian family. I am grateful to Dr. Ross Hayes and Dr. T. E. Lowe for helpful criticism of this paper.

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ILIAC THROMBO-ARTERECTOMY.

By R. P. JEPSON, F.R.C.S., F.R.A.C.S.,

AND

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For those of us who regarded an injured intima as one of the most potent factors of thrombosis, the technique of endarterectomy seemed like a mysterious procedure. I saw one of the early French films on the subject and felt it was a highly traumatizing, incomplete and objectionable method and had not the slightest desire to try it.

—DE TAKATS (1959).

IT is to the credit of the distinguished Portuguese surgeon Cid Dos Santos (1947) that he first recognized the sharp line of cleavage existing between an arterial

ILLUSTRATIONS TO THE ARTICLE BY A. D. McCUTCHEON.

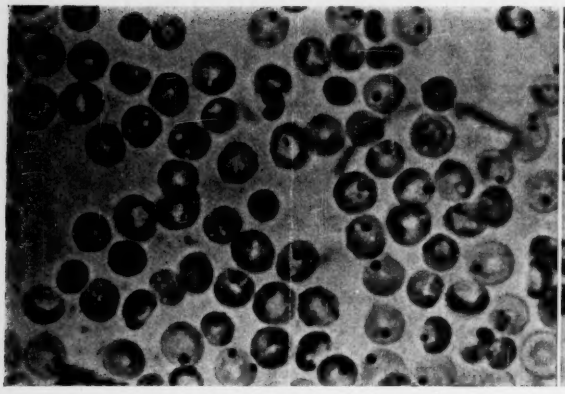

FIGURE I.

Heinz body incubation test. Normal blood showing one large Heinz body and occasionally one or two smaller ones in each erythrocyte. Stained with crystal violet (2%).

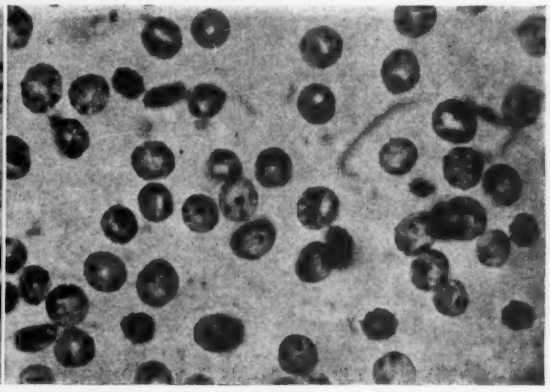

FIGURE II.

Heinz body incubation test in boy with favism; 50% of erythrocytes contained five or more Heinz bodies.

ILLUSTRATIONS TO THE ARTICLE BY R. P. JEPSON AND L. J. OPIT.

FIGURE II.

Arteriogram in Case I. Gross atheromatous involvement of the aorta with complete block of the right common iliac artery from its origin.

FIGURE III.

Pre-operative arteriogram in Case V. Occlusion of right common iliac artery immediately above the take-off of the right internal iliac.

FIGURE IV.

Post-operative arteriogram in Case V. Iliac vessels now patent, with little evidence of generalized atherosclerosis; this illustrates the segmental nature of the disease.

ILLUSTRATIONS TO THE ARTICLE BY J. M. YEATES AND E. HIRST.

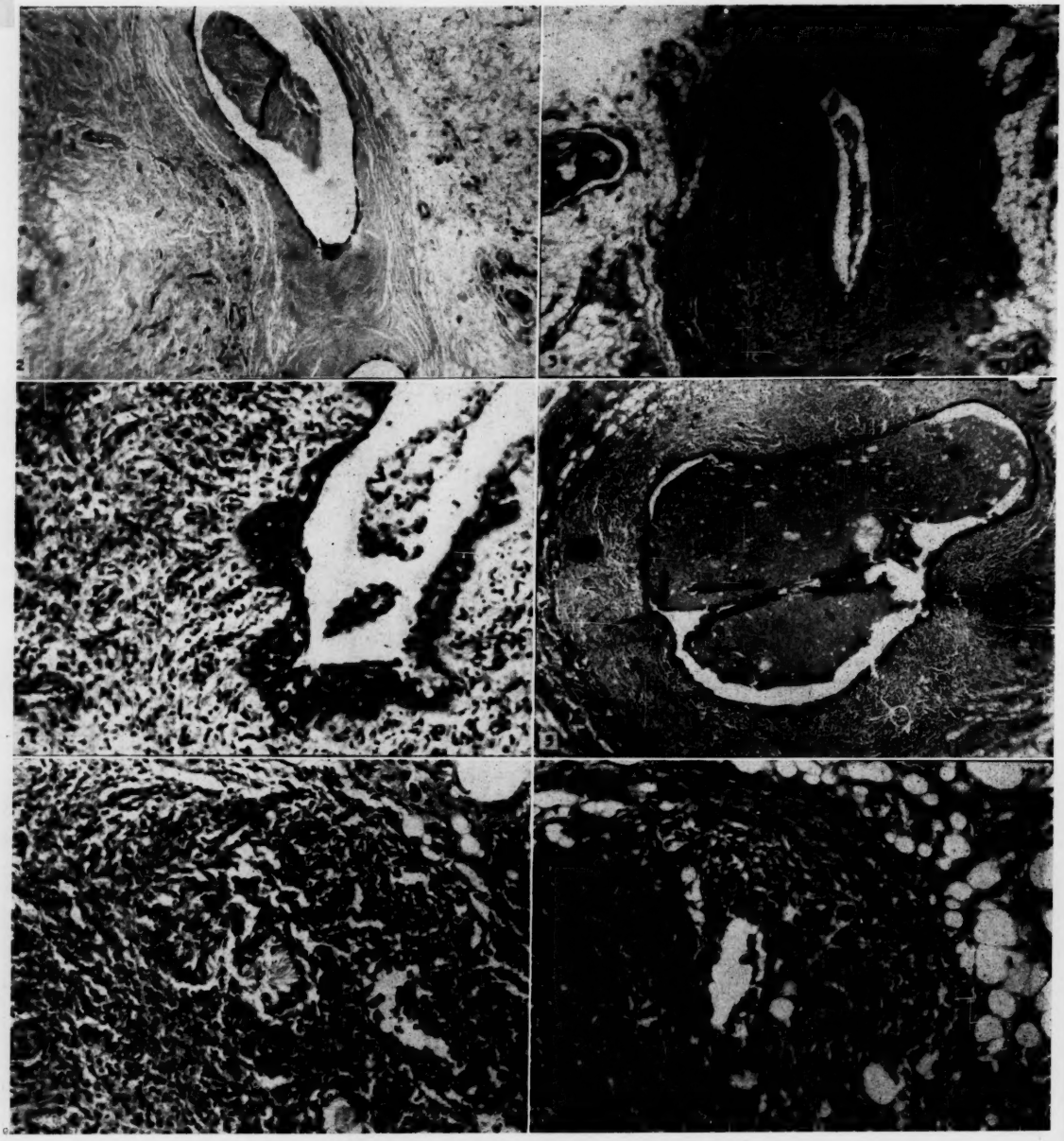

FIGURE II. Case I: Dilated duct with hyaline fibrous wall, attenuated lining epithelium and fatty contents. (×30).

FIGURE III. Case II: Duct with patchy hyperplasia of lining epithelium and an annular zone of inflammatory fibrosis. (×30.)

FIGURE IV. Case II: Higher power photomicrographs of duct shown in Figure III. The inflammatory infiltrate is mainly histiocytic, with scattered plasma cells and lymphocytes. (×118.)

FIGURE V. Case III. Dilated duct with periductal inflammation and fibrosis. The lining epithelium is thin. A crystalline cluster is present in the fatty debris in the lumen. (×30.)

FIGURE VI. Case III: Granulomatous (histiocytic) inflammation reactive to crystalline cluster in the tissues. (×118.)

FIGURE VII. Case III: Giant cells in the inflammatory infiltrate reactive to escaped duct contents. (×18.)

ILLUSTRATIONS TO THE ARTICLE BY C. DUNCAN AND G. BRADFIELD.

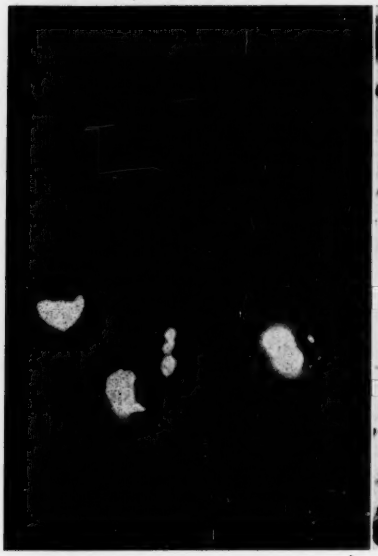

FIGURE I.
Foreign-body giant cells containing anisotropic crystals (low power, polarized light).

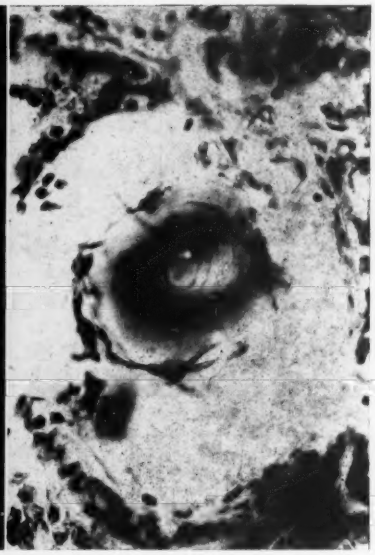

FIGURE II.
Schaumann body showing concentric lamination (medium power, hæmatoxylin and eosin stain).

ILLUSTRATIONS TO THE ARTICLE BY J. S. LEKIAS.

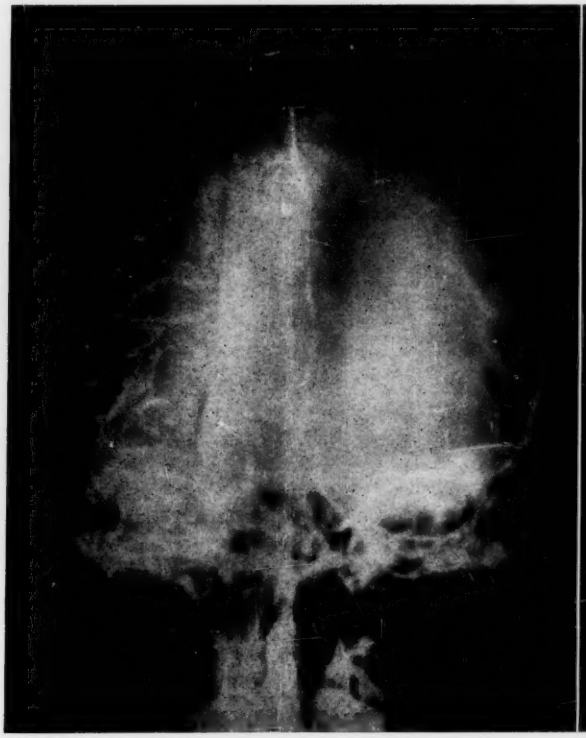

FIGURE I.
Fluid hæmatoma.

FIGURE II.
Solid hæmatoma.

ILLUSTRATIONS TO THE ARTICLE BY GRAEME SLOMAN AND IAN H. McCONCHIE.

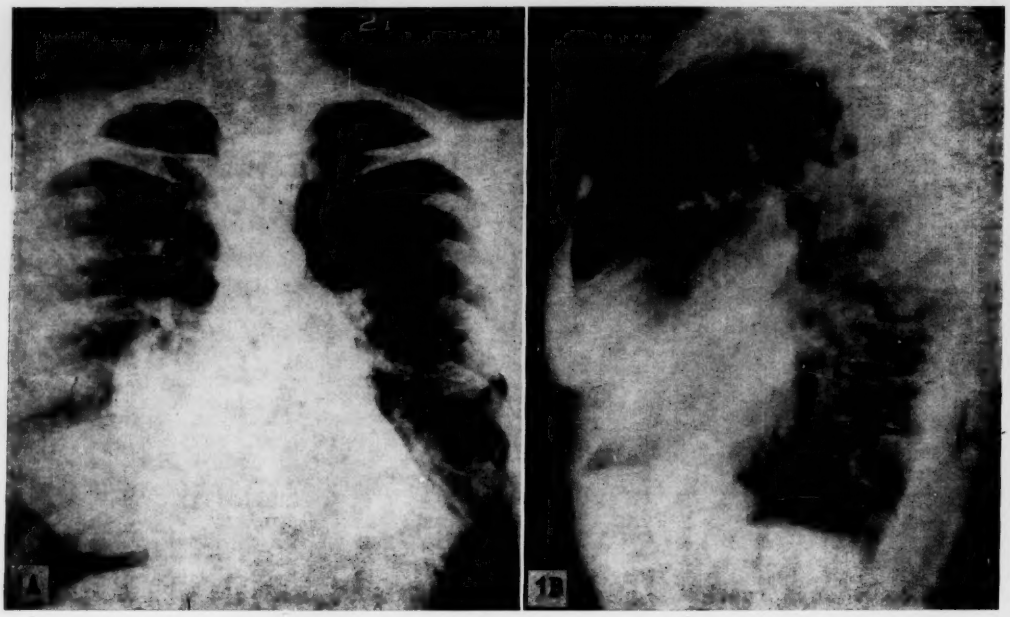

FIGURE I.

X-ray films of the chest when the patient first presented, demonstrating collapse of the middle lobe of the right lung.

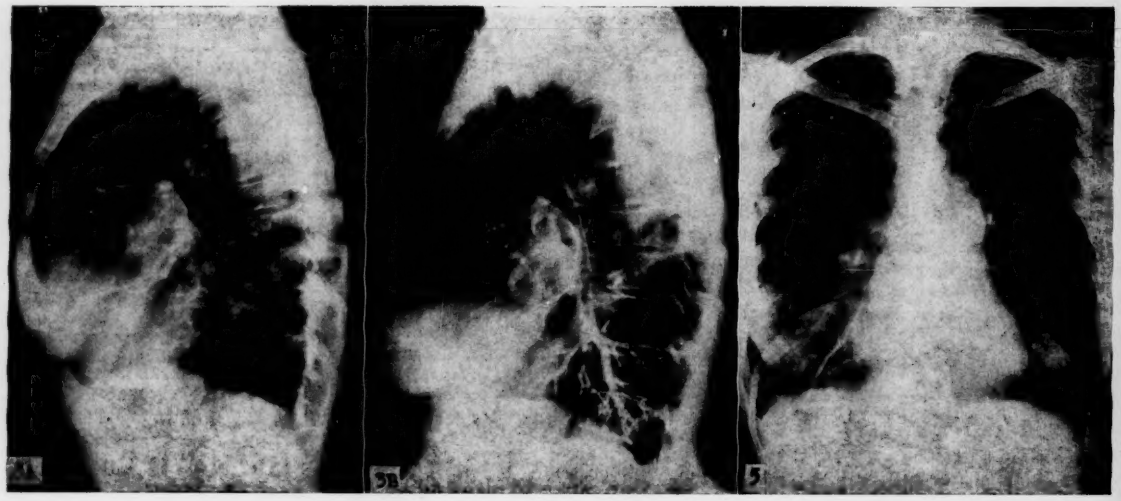

FIGURE III.

A lateral chest X-ray film (A) and bronchogram (B) demonstrating compression of the right bronchus intermedius.

FIGURE V.

Post-operative chest X-ray film demonstrating a reduced cardio-thoracic ratio (17/27 cm. to 13·5/27 cm.) and relatively normal peripheral lung fields.

thrombus and its containing wall. It was he again who applied this finding to the obstructed atherosclerotic artery and described the operation which is alternatively known as disobliteration endarterectomy or thrombo-arterectomy. It was in the following years developed and modified, particularly by French surgeons, most notably Reboul and Laubry (1950); later, many series were published in the United States and the United Kingdom. The results of the operation were not impressive, partly owing to poor selection of cases, faulty techniques and the abuse of anticoagulation. With the advent of the synthetic prostheses, thrombo-arterectomy has been abandoned for use in small vessels or in cases of extensive occlusions. It is our opinion, nevertheless, that disobliteration is an admirable procedure for selected patients, and in particular for those suffering from short segment occlusion, as in the iliac, renal or carotid arteries. It is the purpose of this communication to describe our recent experiences with the former of these sites.

The Iliac Lesion.

The major pathological basis of iliac artery disease is atherosclerosis, and it is evident, as with other lesions due to this process, that the iliac artery thrombosis may be associated with gross lesions elsewhere, or may be an apparently isolated forerunner of what may not become, for several years, a clinically generalized disease. The initial lesion in the iliac vessels is usually a mural thrombosis at or about the level of the take-off of the internal iliac artery. From here the clot thickens with successively deposited layers until the whole of the common iliac bifurcation is involved. Even when occlusion is complete, the thrombus may involve a remarkably short segment of not more than a centimetre or so, and proximal extension, which is much commoner than spread down the external iliac, may be delayed for years. Eventually retrograde spread involves the aortic bifurcation and may, as Leriche pointed out many years ago, move over the fork to pick off the origin of the contralateral common iliac artery. When clotting has occurred in the common iliac, its diameter may become shrunken or remain normal or, alternatively, prior weakness of the wall due to fibrous replacement of the media may leave a fusiform dilatation. The thrombosed artery always shows a mural and peri-arterial inflammation which binds its wall with a varying degree of tenacity to the accompanying vein and the arterial bed.

Selection of Cases.

The main indications for the operation are the symptoms of limb fatigability, claudication, toe gangrene and rest pain; contraindications are general factors which would preclude any major non-urgent abdominal operation, and we are wary of intervening in patients who have associated aortic or diffuse arterial disease of apparently recent onset. Final selection of patients depends on angiography, for which we prefer the Seldinger technique with the catheter introduced in the "good" femoral artery. The angiogram should demonstrate the aorta up to the renal arteries, the iliacs and the femoro-popliteal segment in the involved leg. Lesions which run down the external iliac to below the inguinal ligament or are part of an aortic bifurcation thrombosis are rejected from this type of procedure.

Technique.

Exposure of the aortic bifurcation, together with the involved common and external iliac, is obtained by a mid-line incision reaching from the symphysis pubis to above the umbilicus. The intestines are packed away in the upper part of the abdomen, after which the peritoneum over the arteries is incised and reflected, care being taken that the ureter is defined and protected. In the case of the short segment thrombosis, the common, external and internal iliacs are dissected free from the underlying vein by knife or blunt dissection and controlled with 5-mm. nylon tapes tied over plastic tubes, or with light spring clamps applied at least 2 cm. away from the thrombosed segment. If the lesion is more extensive and runs up to the take-off of the common iliac, then the aorta is freed immediately above the bifurcation; this requires care, as the left common iliac vein is closely applied to its posterior surface and large lumbar arteries course from its postero-lateral surface. After the aorta has been controlled with a clamp, the contralateral common iliac is temporarily ligated, together with the divisions of the thrombosed common iliac. At this stage an incision is made in the anterior wall of the thrombosed segment, which is carried at least a centimetre beyond its limits into the involved artery above and below. Immediately on incision a cleavage line is seen between the organized clot and an outer layer composed of the surrounding adventitia and degenerate media; a blunt dissector shells the clot without difficulty, including a short tail which trails often down the origin of the internal iliac (Figure I). The remaining outer wall is sometimes surprisingly thin, but in our experience is always sufficiently tough to withstand arterial pulsation. At the extremities of the clot, where it approaches the non-occluded wall, the intima tears or tags and leaves a potential site for the development of a dissecting aneurysm. This intimal flap is carefully cut flush with the arterial wall or is sutured into place by a transfixing mattress suture. The arterial field is kept blood-free during these procedures with repeated swillings of normal saline, and flushes of arterial blood from the controlled vessels at each end of the incision are brought about by temporary release of the clamps at approximately ten-minute intervals. If the diameter of the arterial wall at the site of incision is larger than normal, the artery is closed by a continuous over-and-over suture of 4/0 silk. Immediately before the final closure is made, the clamps are again temporarily released and reapplied, and the lumen of the artery is washed out with saline. On completion of the closure, the distal clamp is first let off; if any considerable leak occurs in the suture line, further hæmostasis by through-and-through stitches may be utilized. If, however, as is often the case, the arterial bore at the suture site would be narrowed compared with that of the vessel immediately proximal, we have used a "patch graft".[1] For this a piece of woven "Dacron" or "Teflon" is cut in an oval shape of sufficient length to cover the incision and of sufficient breadth to leave a maximal diameter of about double the previous arterial diameter. This is inserted with a simple over-and-over suture, and in fact creates a small fusiform aneurysm rather than a stricture at the site of repair. The peritoneal flaps are replaced and sutured, and the abdomen is closed with interrupted thread sutures without drainage.

Summary of Results.

CASE I.—A male patient, aged 62 years, had noticed severe claudication in the left leg and thigh after walking about 50 yards for the past year. The limb also felt heavy and tired easily. For the two months immediately before interview he had been confined to his home by severe rest pain in the left foot, which had rendered him sleepless and caused a great loss of weight as well as mental ill-health.

On examination of the patient, his blood pressure was 180/100 mm. of mercury; gross œdema of both feet was present from continued dependency, and tip gangrene of the toes. The left femoral pulse was not palpable; a coarse systolic murmur was heard over the bifurcation of the aorta. Arteriography revealed a complete occlusion of the left common iliac artery down to its division and an additional femoral artery thrombosis at the level of the adductor canal. In addition, the lower end of the aorta showed early aneurysmal dilatation (Figure I).

At operation endarterectomy of the left common iliac artery with left lumbar sympathectomy was performed (Figure II).[2] This man was back at work in two months and has remained well in the 14 months since his operation. His femoral pulse is strongly palpable, the œdema has disappeared and the nutrition of the foot is excellent.

CASE II.—This energetic housewife, aged 59 years, had noticed severe claudication in the right calf and thigh for 12 months.

[1] Following the suggestion of Mr. J. D. Richardson, F.R.C.S.

[2] For Figures II, III and IV see art-paper supplement.

On examination of the patient, her blood pressure was 145/75 mm. of mercury. The right femoral pulse was absent, and there was moderate global atrophy of the right leg. Arteriography revealed a complete occlusion of the right common iliac artery to about 2 cm. below its bifurcation, with an early fusiform dilatation of the left common iliac.

Endarterectomy was performed a year ago. Since operation the patient has had no claudication, and the ankle pulses continue to be of good amplitude.

CASE III.—This man, a retired architect, aged 71 years, had suffered mild claudication for three years in the left leg, and for four years he had noticed mild angina of effort. For the past three weeks he had had severe rest pain in the left foot, of which the left little toe was gangrenous. On examination of the patient his blood-pressure was 150/70 mm. of mercury. At operation, endarterectomy of a clot 5 cm. in length in the left common

FIGURE I.

Specimen of organized clot shelled out from the iliac vessels in Case I.

iliac artery was performed. Excellent pulses were palpable at the ankle immediately after operation, the rest pain cleared and the toe healed without further intervention. This patient is now fully ambulant and pain-free, although handicapped to a degree by angina of effort.

CASE IV.—A male patient, aged 61 years, had severe claudication of the left buttock, thigh and calf, which impaired his abilities as a wage-earner. Nutrition in the foot was good, but no pulses were palpable below the inguinal ligament on the left side.

On examination of the patient, his blood pressure was 150/80 mm. of mercury. The arteriogram showed the aorta to be moderately involved by atheroma, while in the left common iliac artery lay a 3 cm. occlusion. Endarterectomy returned the pulses to the thigh and leg, and the patient is now symptom-free.

CASE V.—This is an excellent example of misdiagnosis. This man, aged 58 years, had noticed that the little toe of his left foot was blue, numb and cold. On reference to a dermatologist, this "lesion" had been treated by superficial X-ray therapy with subsequent necrosis; the resultant ischæmic neuritis caused severe and continual pain. On direct questioning, the patient confessed to claudication in the calf at about quarter of a mile. Five to seven years earlier he had suffered three coronary attacks, from which he had little residue. The right femoral, popliteal and ankle pulses were not palpable, and arteriography showed a short-segment occlusion of the common iliac at the level of the internal iliac take-off (Figure III). This was removed by endarterectomy, and a "Dacron" patch graft was inserted (Figure IV). The toe healed without further intervention, and the patient is still free from claudication.

CASE VI.—This old man, aged 72 years, had a short history of claudication in the right leg over the past two months and five weeks of severe rest pain, and most recently the great toe of the same side had become gangrenous. In addition he had severe angina of effort.

On examination of the patient, his blood pressure was 170/75 mm. of mercury and arteriography showed gross disease of the aorta and a segmental occlusion of the right common iliac artery, as well as bilateral femoral thrombosis in both thighs. The 2 cm. thrombosis in the iliac was removed, and a "Dacron" graft was inserted. This was followed by relief from the rest pain; but unfortunately the patient developed a further coronary attack and died three days after operation.

Discussion.

The distinct advantages of endarterectomy are the speed and simplicity of the operation.

Our results in its use for extensive lesions, using either the direct incision technique described here or multiple incisions and a stripper, have been disappointing; however, with the short-segment thrombosis of the iliac vessels the immediate results are extremely satisfactory, and there is no reason to believe that the long-term follow-up results will be in any way inferior to those of the alternative methods of resection and grafting or the by-pass operation. Its particular advantage would seem to be in the not unusual combination of separate iliac and femoral artery thromboses on the same side causing severe ischæmia, often with rest pain. Such patients are often elderly, with other vascular diseases, such as cardiac ischæmia. In such cases the operation is a calculated risk immeasurably preferable to the inevitable mid-thigh amputation. Recanalization of the iliac vessels enables the collateral circulation to build up sufficient pressure head to reconstitute an adequate foot-flow, and if necessary the readily accessible lumbar chain lying in the paravertebral gutter can be divided with only a few additional minutes to the operation. Such patients with diffuse arterial disease are maintained on long-term anticoagulant therapy commencing five days after operation.

Summary.

1. The patterns of iliac artery thromboses and their development are outlined.

2. The selection of patients for endarterectomy and its technique are described.

3. It is suggested that for this particular problem endarterectomy is at least as successful as any alternative procedure and has many inherent advantages.

Acknowledgements.

We should like to express our thanks to the consultants and practitioners who have referred these patients to us, and to Dr. J. D. Richardson, F.R.C.S., for his suggestion of a patch graft.

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SPILT MILK MASTITIS.

By J. M. YEATES,[1] F.R.C.S., and E. HIRST, D.C.P. (Sydney),

From the Department of Surgery and the Department of Pathology, Sydney Hospital, Sydney.

THE breast condition to be discussed in this paper is most commonly known as plasma cell mastitis (Ewing) or mammary duct ectasia (Haagensen). Similar (or closely allied) lesions have been described in the literature, under a wide variety of names, many of which will be mentioned. Of the names offering, we believe that spilt milk mastitis comes closest to describing both the clinical and pathological picture in most cases. The disease occurs in women, usually middle-aged and parous, who may suffer a fleeting inflammation of one breast. Sooner or later a lump appears, which mimics cancer so closely that needless radical operation may be performed.

[1] Dr. J. M. Yeates' death has been announced since this article was submitted for publication.

Historical Survey.

Courtin (1899), quoted by Cutler (1933) and by Miller (1939), may have been the first to describe the condition as *"un cas de mammite subaiguë simulant une tumeur maligne du sein"*.

Samelson-Kliwansky (1905) described a breast lesion *"Mammacysten mit butterähnlichem Inhalt"* and referred to granulation tissue with giant cells.

Although Ingier (1909) has been credited with one of the earliest descriptions under the title "mastitis obliterans", it is doubtful whether her two cases are representative of this entity.

Bloodgood (1922), in his lengthy paper with the remarkable title "Varicocœle Tumour of the Breast", supplies much clinical detail of cases which often have much in common with the present subject. In his case number 15988, "the clinical signs of carcinoma were definite". Radical mastectomy was performed, and sections showed that the tumour was composed of "tortuous dilated ducts, filled with greenish colloid material, with periductal inflammatory reaction".

Keynes (1924) described "stagnation mastitis", and suggested that the inflammation was due to interference with the escape of products of secretion. He found, however, that in the normal non-lactating breast the mouth of the breast ducts was almost always filled with a plug of keratin.

Cheatle and Cutler (1931) credit Ewing with having used the term plasma cell mastitis in his laboratory, and themselves give a full description of the disease. Adair (1933), by his description of 10 cases, served to establish (or reestablish) the condition as a clinical entity. These three authors all direct attention to an early stage of inflammation, followed by a residual chronic stage, which may persist for years and simulate cancer.

Rodman and Helen Ingleby (1939) consider that plasma cell mastitis, traumatic fat necrosis, lactation mastitis, and infected galactocele are all modifications of the same process. They supply the report of a dramatic case in which radical mastectomy was performed even after examination of a frozen section. They suggest that the lesion is due to enzyme-splitting of milk-like substances, which provoke a reaction in the breasts of non-pregnant women. They produced similar lesions in rabbits by injecting pancreatized milk into the ducts. Their paper is of special interest because of their suggestion that the disease may be unassociated with pregnancy (and lactation), whereas many other authors seek a link.

Cromar and Dockerty (1941) reviewed 24 cases from the Mayo Clinic over 30 years. All the patients were parous; 19 had pain; 20 had skin fixation (three with ulceration); 10 had retraction of the nipple (but in seven the condition was congenital). The correct diagnosis was made only once, cancer being diagnosed on 17 occasions. Nine radical and 15 simple mastectomies were performed on these patients.

Payne, Strauss and Glasser (1943) believe that too much emphasis has been placed on plasma cells: "Plasma cells are merely a cellular expression of the chronicity of an inflammation . . . "

Gaston (1947) describes a case in which there was a blood-stained nipple discharge—one of the very few in the literature. He advises simple mastectomy.

Newton (1947) appears to have published the first report in Australia. He points out that in all previously reported cases the patients were parous, and the average age was 36 years. His two patients were nulliparæ, and their ages were 58 and 62 years respectively. This is of considerable interest, as it shows that the escaping duct secretion which arouses the granulomatous reaction is not necessarily the milk of lactation. In one of Newton's cases, heaping of the duct epithelium led to radical mastectomy even after examination of a frozen section. He advises simple mastectomy.

Cutler (1949) reported a case in which the second breast became similarly affected after an interval of nearly seven years. This appears to be the only recorded case of bilateral involvement.

Haagensen (1956) provides an excellent account of the condition in his textbook.

Ackland (1958), writing under the title "Chronic Inflammatory Mastitis with Duct Ectasia", suggests that the condition may be not so rare, some cases being labelled chronic mastitis.

Reports of Cases.

Case I.—Mrs. A., aged 59, years was referred by Dr. E. C. Palmer, of Forbes. She had noticed by chance a lump in the left breast on December 3, 1959. She denied any other symptoms, and was emphatic that there had been no pain or redness. The menarche had occurred at the age of 11 years, and menstruation had been of the 3/28-day pattern, and regular. She had had two miscarriages, and three living children, only one of whom had been breast-fed for any length of time, the supply being poor at the first and third lactations. The breast pump had been used at the last lactation (1932). The menopause had occurred naturally in 1950.

Examination of the patient showed that the breasts were rather large (size 5 in scale 1 to 7). The nipples and areolæ were normal, and no secretion could be obtained by compression. There was a firm (but not hard) irregular lump at the 11 o'clock position near the edge of the left areola. It measured 1·5 cm., and was quite superficial and fairly well defined. There was no fixation, and the axillary nodes were not palpable. The remainder of the breast and the entire right breast were normal. Biopsy-excision was performed on December 10. The breast tissue surrounding the lump was normal, and no dilated ducts could be seen. Examination of the cut surface of the lump showed three or four grossly dilated ducts, and on squeezing the specimen cheesy material exuded. Examination of a frozen section confirmed the diagnosis of "duct ectasia". Whilst the report was being awaited, the margins of the circumareolar incision were retracted, and the remaining ducts were studied. They did not appear dilated.

The final pathological findings were as follows:

> The specimen was a piece of breast tissue 5·0 × 2·7 × 2·4 centimetres. The cut surface showed a relatively well defined firm ovoid nodule 2·2 × 1·6 × 1·5 centimetres, in which clusters of thick-walled dilated ducts were present. The ducts measured each approximately 0·6 centimetres in diameter, and were filled with inspissated secretion of the consistency of cream cheese. The surrounding breast tissue was firm. No dilated ducts were found in it.
>
> Sections show that the ducts are dilated, and contain abundant lipoid debris and a few clusters of fatty acid crystals. The duct epithelium is attenuated, and in a few places is replaced by a narrow zone of calcification. The walls are composed of hyaline practically acellular fibrous tissue. There are rare foci of lymphocytes and a few collections of pigment-laden histiocytes near the duct walls, but there is no evidence of escape of duct contents into surrounding breast tissue.

Case II.—Mrs. B., aged 60 years, referred by Dr. Peter Broughton of Sydney, said that on June 23, 1959, she had noticed one spot of bright blood on her brassière in relation to the left nipple. On June 30, a similar but larger spot appeared. She saw no blood on the nipple. On compression of the breast no discharge appeared, but the breast felt tender, especially in the lower half. During that day throbbing was felt, and the sensation of something "gathering". Pressure of clothes aggravated the pain. Later in the day redness appeared, at first round the nipple, but soon spreading to much of the breast proper. She slept poorly that night, and the next day found the symptoms more marked, the redness now being very prominent. The next night the inflammation subsided somewhat, without any treatment, but was still marked when she was seen by Dr. Broughton on July 6.

On July 7 the pain had gone, but the tenderness remained. The breasts were seen to be of average size (size 4), and the right breast appeared normal. There was a fading flush on both inner and outer aspects of the left breast, the colour being a mixture of blue and red. The nipple and areola were normal, but there was tenderness under the lower part of the areola, and here also was a patch of induration 2 cm. in diameter. The overlying skin was neither œdematous nor fixed. A nipple discharge could not

be produced, and the axillary nodes were not enlarged. The patient said that the menarche occurred at the age of 12·5 years. The menses had always been regular and of the 5/28-day pattern. The menopause had occurred naturally at the age of 45 years. She had two children, aged 31 and 26 years respectively; both had been breast fed for four months, when poor milk supply called for weaning. There were no complications of lactation, and the breast pump was not used. There had been no other pregnancies. The patient was fearful that she had breast cancer. For this reason she was insistent upon immediate biopsy. This was performed on July 13. A curved subareolar incision was made. The breast tissue was seen to consist largely of dilated ducts, filled with fluid like dark honey. All abnormal tissue was excised and the wound was closed by suture without drainage. Examination of a frozen section showed "duct ectasia".

The final pathological findings were as follows:

> Specimen was a nodule of breast 8 × 6 × 5 centimetres. The cut surface showed abundant adipose tissue with thin strands of breast tissue. Throughout the tissue, dilated ducts with a brown lining and measuring up to 0·3 centimetres in diameter were present. Many of these ducts could be seen as vein-like structures of pale blue colour.
>
> Sections show dilated ducts, some of which contain a little debris and a few pigment and lipoid-laden histiocytes. The lining of the ducts is uneven with small areas of slightly hyperplastic epithelium. There is notable periductal inflammatory infiltrate with fibrosis. Histiocytes and lymphocytes are predominant. There is no evidence of malignancy.

In view of the inflammatory signs in this breast, it is worth recording that the wound healed quickly and well.

CASE III.—Mrs. C., aged 38 years, referred by Dr. Stafford Marsh of Kempsey, had noticed a small lump near the right nipple on October 5, 1959. There had been no symptoms whatsoever prior to this. The lump was painless, and there was no nipple discharge. The patient had one child, aged 10 years, who had been breast-fed for only six weeks because of poor supply. There had been soreness and cracking of the nipples, but no breast inflammation. There were no other pregnancies. The menarche had occurred at the age of 14 years, and the menses had been regular and of the 4/35-day pattern. The last menstrual period had occurred on October 26, and was 19 days overdue. However, the patient was not pregnant.

Examination on November 5 showed that the patient was a very heavy woman, whose breasts were excessively large (size 7). Just beyond the edge of the 5 cm. areola of the right breast was a lump 1·5 cm. in diameter in the 12 o'clock position. This was firm, but not hard, and was quite superficial. It was somewhat irregular, and not clearly defined. There was no skin or areolar fixation, and no nipple discharge. The axillary nodes were not enlarged. Biopsy via a circumareolar incision was performed on November 6. When the lump was approached, a sudden gush of thick cheesy fluid appeared. Dissection showed that the terminal milk ducts were dilated and bluish, and on being cut exuded the same fluid. All pathological tissue was excised, the wound being sutured without drainage. Examination of a frozen section showed no evidence of malignancy.

The final pathological findings were as follows:

> The specimen was a plaque of breast tissue 5 centimetres in diameter and 1·5 centimetres thick, together with several smaller pieces. Throughout the tissue there were dilated ducts, distended with cheesy material. These ducts were hard before opening. Sections show dilated ducts containing abundant debris with a few lipoid-laden histiocytes. The lining of the ducts is slightly variable with some areas of hyperplastic epithelium. In most of the dilated ducts the epithelium is attenuated, and in a few it is absent. There is severe periductal inflammation in which histiocytes are pre-dominant. Foci of plasma cells are also present and there are a few scattered lymphocytes. A striking feature is the pronounced granulomatous reaction around escaped duct contents in which fatty-acid crystal clefts can be found in places.

The wound healed by first intention, the patient being discharged on the fourth day.

Discussion.

These three cases illustrate the stages of the disease, which we have attempted to summarize thus:

Stage I: Duct ectasia (no symptoms).

Stage II: (*a*) Quiet leak (no symptoms).
(*b*) Sudden perforation (symptoms of acute inflammation).

Stage III: Residual tumour (following either (*a*) or (*b*)).

Case I seems to be an uncomplicated picture of Stage I. There was no seepage into the stroma. There were no symptoms until the dilated ducts themselves were large enough to cause a local painless lump, which aroused suspicion of carcinoma. Grossly at operation the cut surface showed a relatively well defined nodule, in which dilated ducts were easily seen (Figure I). The problem now became one of excluding duct carcinoma.

Case II is an example of Stage II (*b*). There were two possibilities of diagnostic error—firstly, acute (bacterial) infection, and secondly, the dreaded inflammatory carcinoma. For a few days the latter was seriously considered. We found that a few days spent in clinical observation at this particular phase (as advised by Cutler, 1931) was valuable. Such a short delay is not likely to affect the prognosis of inflammatory carcinoma if it is present.

Case III is an example of Stage III evolving from a quiet leakage of duct contents (Stage II (*a*)). Here it was necessary to exclude duct carcinoma with infiltration.

It is worthy of note that none of our three patients had reached the ultimate stage when severe and extensive fibrosis causes nipple retraction.

The gross appearances in the affected part of the breast varied with the stage of the disease. In the earliest stage (Case I, Figure I) there were dilated ducts clustered to form a firm nodule. Cheesy or milky material was expressed or exuded from them. At this stage the gross appearances may be identical with those of the uncommon comedo carcinoma (intraduct carcinoma without infiltration). At a later stage (Cases II and III) the dilated ducts were still present, and there was periductal induration extending in variable degree into the surrounding

FIGURE I.

Case 1: Cut surface, showing dilated ducts with cheesy contents. A large duct is present near left-hand edge.

breast tissue. This appearance may closely resemble the relatively common intraduct and infiltrating carcinoma (duct carcinoma with infiltration). In the advanced stages of the disease (Cromar and Dockerty, 1941), the appearance of duct ectasia may be obliterated, and the resulting lump, skin fixation and enlarged lymph nodes are very suggestive of scirrhous carcinoma.

Microscopically we had no great difficulty in excluding carcinoma in our cases. The dilated ducts contained amorphous and crystalline fatty material and lipoid-laden histiocytes. The epithelial lining of the ducts was almost always attenuated. Rarely part of the duct was lined by hyperplastic epithelium composed of darkly-staining cells. Some of the histiocytes within the ducts also had darkly-staining nuclei (Figure IV).[1] We emphasize these features on account of the difficulties of diagnosis on examination of frozen sections that have been referred to by Adair (1933), by Rodman and Ingleby (1938), by Newton (1949) and by Stewart (1950). On the other hand, frozen section diagnosis has been entirely reliable in Haagensen's (1956) later cases.

Inflammatory reaction in the walls of the ducts and in the surrounding breast tissue was present in two of our cases. It was mainly histiocytic. The histiocytes contained fat and surrounded crystalline (fatty acid) clusters (Figure VI) near the ducts and at some distance from them. In a few places giant cells were present in the inflammatory infiltrate (Figure VII). This feature has led to a false diagnosis of tuberculosis (Cromar and Dockerty, 1941). (The condition has been called pseudo-tuberculosis of the breast.)

In these latter cases, plasma cells and lymphocytes were present in the inflammatory infiltrate. Instances in which plasma cells predominated are described usually under the title "plasma cell mastitis". It is now agreed that such a histological picture is only one (probably late) stage of the disease (Payne, Strauss and Glasser, 1943).

Diagnosis.

Although the clinical patterns in these three cases were different, there were certain features which suggested the diagnosis of spilt milk mastitis. The lesion was situated near the nipple, was firm, and lacked the characteristic hardness of scirrhous carcinoma. Although these features are not diagnostic, they are enough to warrant the inclusion of the condition in the differential diagnosis. This discipline will help to prevent needless radical operations such as abound in most other reports. In this we differ from Ackland, who believes that attempt at clinical diagnosis is futile.

Treatment.

Cheatle and Cutler state that the process subsides very slowly. Cassie (1953), having established the diagnosis by biopsy, allowed the lesion to remain and subside. Gaston (1947) and Newton (1949) advise simple mastectomy. Our experience leads us to agree with most authors who advise confirmation of the diagnosis by biopsy and excision of the lesional tissue. Such treatment does not appear to be followed by difficulty in healing or recurrence. Our patients were treated recently, and so far are free of complications. The wounds healed by first intention, presumably because any inflammation present was chemical in origin.

Summary.

1. Three parous women, not pregnant or lactating, presented with lesions near the nipple. Two had lumps. One had inflammation with an area of induration.

2. At operation, all the patients had lesions characterized by dilated ducts containing secretion.

3. Pathological examination showed that the dilated ducts contained amorphous and crystalline fatty material. In two of the lesions there was notable inflammatory fibrosis. Evidence of escape of duct contents into the tissues was found.

4. These lesions represent three stages of a disease process which is due to accumulation of secretion in the ducts with subsequent escape.

5. In any stage the clinical and gross appearances may simulate some form of carcinoma.

6. A clinical diagnosis should be attempted and confirmed at biopsy.

7. Excision of lesional tissue is advised.

8. The name spilt milk mastitis is preferred.

[1] For Figures II to VII see art-paper supplement.

Acknowledgements.

We wish to thank Dr. Alan Palmer, Kanematsu Memorial Institute of Pathology, Sydney Hospital, for his helpful advice and criticisms. Dr. Siegfried Fink has been most obliging in translations of the German references. We are grateful to Miss J. Ashby, Librarian, for her assistance in obtaining the references.

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Addendum.

Since this article was written we have had the opportunity, by courtesy of Dr. S. L. Spencer, to study another patient suffering from spilt milk mastitis. On this occasion aerobic and anaerobic cultures of the excised tissue were made, but they yielded no growth.

SOLID SUBDURAL HÆMATOMA.

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WITH the increased use of cerebral angiography in patients with traumatic cerebral conditions, a hitherto ill-defined group of subdural hæmatoma is emerging with greater definition. It is the purpose of this communication to report and analyse 19 cases of solid subdural hæmatoma treated by the neurosurgical unit of the Royal Perth Hospital between July 1, 1955, and June 30, 1958.

Classification.

In the writer's opinion, it is perhaps wrong to call these hæmatomata anything but acute, since it would seem from what follows that the bleeding responsible for the hæmatoma occurs at the time of, or very soon after, the injury; therefore the temporal classification is relative to the time of diagnosis, but the lesion is probably present *ab initio*.

Statistics.

The Royal Perth Hospital deals with some 500 cases of head injury *per annum*. These are largely made up of traffic, industrial and miscellaneous accidents, in which alcohol plays a considerable part. Over this period of three years, about 1500 patients with head injuries have passed through the hospital. The more severely injured patients are admitted from other metropolitan or country hospitals, which means that the Royal Perth Hospital serves the entire State under certain circumstances. From this total, 52 cases of intracranial collections have been found as follows: (i) 19 solid subdural hæmatomata; (ii) 13 cystic hygromata; (iii) 11 fluid subdural hæmatomata; (iv) nine extradural hæmatomata.

A total of 146 patients have been submitted to surgery because of their head injury, 52 for intracranial collections (35%) and 35 for depressed or compound fractures of the skull (24%); the remainder had exploratory burr holes made either because of the gravity of the patient's state on admission to hospital, when acute hæmorrhage was suspected, or because of failure to improve during conservative treatment.

The practice of making exploratory burr holes was carried out during the first eighteen months of this survey, but has now almost entirely been replaced by carotid angiography.

Further analysis with regard to the radiological presence of fractures in the 19 patients with solid hæmatomata shows that 11 had fractures and eight did not; of those with fractures of the skull, the hæmatoma was on the opposite side from the fracture in seven patients (Table I). Sixteen patients had the hæmatoma mainly over the temporal surface of the brain, and only two patients and one patient respectively had the hæmatoma over the frontal and parietal surfaces. This does not mean that the lesions were exclusive to any one site, but that it was considered at operation that the initial hæmorrhage had occurred in these areas.

Pathological Considerations.

That these hæmatomata are the result of severe head injury is undoubted. The motion of the brain when subjected to alteration in its velocity is such that it moves upon and is lacerated by the uneven surface of the floor of the middle and anterior fossæ, as well as impinging upon the lesser wing of the sphenoid bone. The movement is bilateral and rotational, with shortening of one group of veins and lengthening of another; the veins principally affected are those draining into the spheno-parietal sinuses. In the majority of cases the disruption of these veins and the cerebral surface is the cause of this type of collection. To define the subdural space therefore is unnecessary; suffice it to say that the hæmatomata occur deep to the dura and superficial to the cerebral surface, and if the cortex is lacerated, the subdural hæmatoma may be related to small or large intracerebral hæmatomata. On the other hand, the fluid variety is found on the convex parietal surfaces in relationship to veins draining into the superior longitudinal sinus. The essential difference between the two types of collection appears to be that in the fluid variety the accumulation is the result of a slow extravascular increase of blood between the dura and the brain, often over a prolonged period of time, and often without significant trauma and without disruption of cerebral tissue. The collection remains fluid because the clotting mechanism is not initiated. However, in the solid variety bleeding is immediate and sometimes continuous. The source of the bleeding is probably twofold—the veins draining into the sinuses and the vessels of the disrupted cerebral cortex. It is this cortical disruption that initiates the clotting mechanism, and in any one of these hæmatomata it is not unusual to find black fluid blood, usually not more than one ounce, solid hæmatoma of varying age, and the vessel or vessels from which the hæmorrhage occurred still bleeding. In Case 18 of this series, this vessel was a superior temporal artery which recommenced bleeding with the removal of the hæmatoma.

Reference to Table I will indicate the age and sex incidence of this type of hæmatoma. No instance of this lesion has been met in children, and since this unit is responsible for the treatment of neurosurgical conditions at both the Royal Perth Hospital and the Princess Margaret Hospital for Children, it seems that this condition is uncommon in children.

To summarize the statistical and pathological considerations, it appears that the solid subdural hæmatoma is predominantly the result of severe head injury, that it occurs mainly in males between the ages of 30 and 60 years in the temporal region, and that if a fracture is present then the majority of the hæmatomata tend to occur on the side opposite to the fracture.

Clinical Considerations.

Not one of these patients could give a history because of impairment of consciousness; six were completely inaccessible, and the remaining 13 were disorientated to the degree that their statements could not be taken as accurate (Table II). This contrasts with the fluid type of hæmatoma, in which the patient is frequently able, in the early stages, to give a coherent history.

All the patients of this group suffered severe head trauma, all presented signs of cerebral damage to a varying degree, apart from their altered conscious state. In Case 8, although it is stated that mental and social derangement were the only preoperative findings, clear papillœdema was present.

The important result of the variety of physical findings is that a strong suspicion is raised of increased intracranial tension and cerebral damage.

Once this suspicion occurs, the diagnosis is reasonably easy to reach, provided the history of trauma is available. Case 10 caused considerable confusion, as no history of trauma was obtained and no evidence of trauma was evident until an X-ray examination of the patient's skull revealed a fracture. Once the two factors of trauma and altered consciousness are available in the history of the patient, then the possibility of a solid subdural hæmatoma should be considered and carotid angiography undertaken. Immediate investigation becomes imperative, as the danger of tentorial herniation (if not already present) is considerable. This danger makes the performance of lumbar puncture extremely hazardous; it does not yield any information, and it greatly increases the risks. In this series, six patients were admitted to hospital unconscious, and four of these had become unconscious after ill-advised lumbar puncture prior to their admission.

Table I shows the time interval between the accident and the operative treatment. From Cases 1 to 6 the condition was not suspected in most instances. One patient (Case 1) was admitted from a mental institution. Another (Case 2), a well-known alcoholic with peculiar habits, was found in a gutter unconscious and admitted to hospital. He continued to behave peculiarly on regaining consciousness, and the writer, who was responsible for his care, became suspicious only after an epileptiform seizure and subsequent left hemiparesis had occurred. A third patient (Case 3) became unconscious after lumbar puncture. A fourth (Case 6), again in the writer's care, appeared to be improving except for his mental state which prompted angiography. It will be seen that from Case 6 onwards the members of the department were more aware of the condition, and tended to make an arteriographic investigation at a much earlier stage and more frequently.

TABLE I.

Case Number.	Year.	Sex.	Age. (Years.)	Side of Fracture.	Side of Hæmatoma.	Interval from Trauma to Operation.[1]	Site.	Result.
1	1955	M.	45	—	Left.	30+	Temporal.	Good.
2	1956	M.	47	Right.	Right.	31	Temporal.	Good.
3	1956	M.	41	Right.	Right.	30+	Temporal.	Bad.
4	1956	M.	21	Right.	Left.	12	Temporal.	Good.
5	1956	M.	24	—	Left.	13	Temporal.	Good.
6	1957	M.	67	—	Left.	28	Temporal.	Bad.
7	1957	M.	28	Right.	Left.	3	Temporal.	Good.
8	1957	M.	43	Left.	Right.	9	Frontal.	Good.
9	1957	M.	34	Right.	Left.	6	Frontal.	Good.
10	1957	M.	69	Left.	Right.	17	Parietal.	Good.
11	1957	M.	31	Right and left.	Right.	11	Temporal.	Good.
12	1957	M.	48	Left.	Left.	3	Temporal.	Good.
13	1957	F.	46	—	Left.	1	Temporal.	Died.
14	1957	M.	53	—	Left.	? 4	Temporal.	Good.
15	1957	F.	67	—	Left.	8	Temporal.	Died.
16	1957	M.	26	Right.	Left.	3	Temporal.	Good.
17	1957	M.	47	Left.	Right.	1	Temporal.	Good.
18	1958	F.	50	—	Right.	30	Temporal.	Doubtful.
19	1958	M.	33	—	Left.	15	Temporal.	Good.

[1] Average, 13 days.

Diagnosis.

The diagnosis was that of raised intracranial tension from a space-occupying lesion, and the differential diagnoses considered were subdural hæmatoma, intracerebral hæmatoma or subdural hygroma. Except in Case 3, in which the gravity of the situation demanded immediate decompression, all patients were subjected to arteriography. The findings from arteriography are definite; reference to Figures I and II[1] will show that in the fluid variety the depression of the cortex from the inner table of the skull is smooth, well-defined and pond shaped, with the brain reaching the inner table of the skull at the superior and inferior limits of the depression, whereas in the solid hæmatoma the depression is less well defined and causes a less marked depression of the cortex. I am indebted to Dr. A. Merritt for the interpretation which follows. He points out that in the fluid hæmatoma, which is of gradual onset and often of considerable volume, the brain is gradually depressed antero-posteriorly. Therefore on radiographic plates taken in antero-posterior projection this depression is seen as a clear-cut deficiency with the upper and lower limits well defined, whereas in the solid type which gradually fades out at its periphery, the brain comes back to the surface and gives the impression of shallowness; that is, the fluid variety tends to be shaped like half a cylinder, and the solid type like a saucer. The time interval between the accident and the diagnosis differentiated between extradural and subdural hæmatomata.

TABLE II.

Condition on Admission to Hospital.[1]

Case	State of Consciousness.	Eye Signs.	Aphasia.	Motor Signs.	Plantar Reflexes.[2]
1	Disorientated.	—	Aphasia.	Epilepsy.	R↕ L↓
2	Disorientated.	—	—	Left hemiparesis.	L↑ R↓
3	Unconscious.	—	—	Left Jacksonian.	L↑ R↑
4	Disorientated.	Papilloedema.	Motor aphasia.	—	R↑ L↓
5	Disorientated.	Diplopia.	Aphasia.	Convulsion.	R↓ L↓
6	Disorientated.	—	Aphasia.	Right hand weak.	R↕ L↓
7	Disorientated.	Papilloedema.	Aphasia.	—	R↓ L↓
8	Disorientated.	Papilloedema.	—	—	R↓ L↓
9	Unconscious.	Right dilated pupil; papilloedema.	—	—	R↑ L↑
10	Disorientated.	Right ptosis; ? papilloedema.	—	Right facial palsy.	R↓ L↓
11	Disorientated.	—	—	—	R↓ L↓
12	Disorientated.	—	—	—	R↓ L↓
13	Unconscious.	—	—	—	L↑ R↓
14	Disorientated.	Papilloedema; sluggish pupils.	—	Left-sided weakness.	L↕ R↓
15	Unconscious.	—	—	Mid-brain fits.	R↑ L↑
16	Disorientated.	—	Motor aphasia.	—	R↑ L↓
17	Disorientated.	—	—	Left hemiparesis.	R↓ L↑
18	Unconscious.	Divergence.	—	Right facial palsy; right limb palsy.	R↑ L↓
19	Unconscious.	Papilloedema.	—	Left Jacksonian; left palsy.	R↑ L↕

[1] Six patients were admitted unconscious from other wards or hospitals.
[2] ↑, upgoing; ↓, downgoing; ↕, equivocal.

[1] For Figures I and II see art-paper supplement.

Management.

Once the diagnosis was made, all patients were transferred to the operating theatre, where the hæmatoma was evacuated. It is impossible to remove these hæmatomata adequately through a burr hole. In each case an osteoplastic flap was fashioned and the entire hæmatoma removed under vision. In addition, hæmostasis was more certainly achieved and all necrotic and softened brain adequately removed. If the brain failed to rise to the level of the dura after removal of the clot, lumbar puncture was performed and Ringer's solution injected into the thecal space until the pressure read 120 mm. or the brain came to the surface. The wound was then closed without drainage, and if the patient had been unconscious prior to operation, tracheotomy was performed and an intragastric tube was inserted.

Results.

Reference to Table I will show that we had two deaths, two bad results, and one doubtful result, although the patient is now improving. The other results were classed as good if the patients returned to the state they were known to be in prior to the accident. One patient (Case 3) was certified insane; another (Case 6) has remained hemiplegic and aphasic, and is now languishing in a chronic invalids' hospital; a third (Case 13) died without regaining consciousness, and at autopsy she was found to have a large extradural abscess; a fourth (Case 15) died eight months after the accident in another hospital, again without ever regaining consciousness. In Case 2 the result is classed as good, although that patient too was certified insane; but he had spent a considerable time prior to his accident in and out of either the police cells or a mental receiving home. There have been in this series two cases of post-traumatic epilepsy (Cases 4 and 12). It will be seen, therefore, that the prognosis for the condition on this small series is not encouraging—in six of the 19 cases the results are bad.

Discussion.

Although as a pathological and clinical entity this condition must be as old as head injuries, it is the

advent of arteriography which has thrown it into bold relief, because the condition, from this series at least, appears to be the commonest post-traumatic intracranial collection. The diagnosis depends upon suspicion when the patient fails to improve after two or three days, or upon the continuance of unconsciousness after his admission to hospital; arteriography should be undertaken in the treatment of any head injury in which hypothermia is considered, and it is the practice of this clinic to exclude a space-occupying lesion by arteriography before embarking upon hypothermia for head injuries. The condition is dependent upon the rupture of basal veins, by which is meant veins draining the temporal rather than the parietal surfaces of the brain, and on the molecular disruption of the cortex. The prognosis appears to be serious, in that in over six of our cases the results were unsatisfactory; but nine of the patients were chronic alcoholics, and in any branch of medicine alcohol adversely affects the prognosis. In addition, a considerable proportion of the patients were in the older age group, and this, too, adversely affects the outcome.

This is a relatively common condition, which requires early diagnosis and urgent treatment.

Summary.

1. Nineteen cases of solid subdural hæmatoma are presented.

2. In the writer's view, these hæmatomata occur mainly after severe head injury; they arise in the temporal region as a result of a breach in the vascular tree and the cerebral surface, with resulting release of the clotting mechanism.

3. Six of the results are bad, in that two patients died and two failed to make complete neurological recoveries. A further two suffered from post-traumatic epilepsy.

4. The condition appears to be best treated by formal craniotomy, tracheotomy, and the full routine for the nursing of the unconscious patient.

Acknowledgements.

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CAVAL INFUSION BY THE SELDINGER TECHNIQUE IN THE TREATMENT OF RENAL FAILURE.

By VERNON MARSHALL, F.R.A.C.S.,
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THE principles of conservative management of oliguric renal failure are well established and entail the restriction of fluids and electrolytes to that amount required for the replacement of insensible losses, and the provision of an adequate caloric intake to minimize protein catabolism (Merrill, 1955).

In a normal person, maximum protein sparing can be achieved with an intake of 100 grammes of carbohydrate per day (Gamble, 1947), but in patients with renal failure this is probably not sufficient, and an intake of over 250 grammes of carbohydrate yielding 1000 Calories daily should be aimed at (Bull, 1955).

In practice, the task of providing sufficient calories in as little as 400 ml. of fluid presents a major problem. There are 1000 Calories in 500 ml. of 50% glucose solution, but few patients can tolerate feeding with such a solution for any length of time. Sucrose and lactose are only slightly more palatable. Nausea, vomiting and diarrhœa are frequent sequelæ of oral feeding with these hypertonic solutions, even if a gastric tube is employed.

Diarrhœa, besides adding to the patient's discomfort, also makes the accurate collection of urine specimens more difficult. For such reasons, the caloric requirements must be determined by the tolerance of the patient to a particular diet, and some modification of the Borst régime (Borst, 1948; Kolff, 1952) is usually employed.

Severe and intractable nausea, however, will often render oral feeding impossible, and for patients after operation oral feeding may be contraindicated. In these instances, parenteral feeding will be required. The advantages of parenteral feeding are that it is capable of precise control and is less tiring to the patient. Against the advantages must be weighed the dangers, which are not inconsiderable.

A hypertonic solution, such as a 50% solution of glucose, will rapidly induce thrombosis if delivered into a peripheral vein, and must accordingly be given into a large venous channel where rapid dilution of the fluid will occur at the tip of the cannula. This entails delivery into the innominate vein or superior vena cava if the upper limb is used, or into the iliac vein or inferior vena cava if the saphenous vein is cannulated. The major risks of these techniques are thromboembolism and infection, and on this account, although some authors have reported series free of complications (Shaw, 1959), caval infusion has not found universal acceptance (Taylor, 1957).

Thromboembolism may be minimized by the addition of heparin (3000 units) and alcohol (20 ml. of a 70% solution) to each 500 ml. bottle. This will help to prevent thrombosis in the cannula and in the vein near the tip of the cannula. However, deposition of fibrin around the outside of the length of cannula contained within the lumen of the vein is difficult to prevent, and has been noted on several occasions at autopsy, and also by previous workers (Indar, 1959). When the cannula is removed, the accumulated fibrin may be left within the vein and become dislodged to form an embolus. For this reason it is preferred to use the shorter pathway to a large venous channel provided by the femoral vein, and to insert the cannula no more than 8 cm. into the iliac vein.

Infection is more likely to develop when the vein is exposed by a cut-down technique, and many methods of percutaneous introduction of cannulæ have been suggested.

A fine-bore "Polythene" catheter can be introduced through the lumen of an 18-gauge needle after venipuncture of the femoral vein; but this severely limits the size of the catheter, so that stasis and clotting are more likely to occur.

The alternative method of using the "Polythene" catheter as a sheath around an intravenous needle, the tip of which projects just beyond the end of the catheter, enables a larger size of catheter to be used (Massa *et alii*, 1950). This technique is readily applicable to subcutaneous veins of the arm, but would probably be difficult with the femoral vein.

The technique described by Seldinger (Seldinger, 1953), using a flexible steel wire introduced by percutaneous puncture into a vessel to guide a tapered catheter into the lumen, has been extensively employed in arteriography (Luke, 1958). The method is readily applicable to venous cannulation, with the use either of an arm vein or the femoral vein at the groin, and the catheter can be of considerably larger bore than the introducing needle. Briefly, the method consists of inserting a needle surrounded by a closely-fitting steel cannula into the vessel (Figure I). The needle is then removed and a long, flexible, stainless steel wire is passed into the lumen of

the vessel through the cannula. The cannula is then removed, and over the outside of the guide wire is passed a "Polythene" catheter, the tip of which is bevelled to fit the guide wire. The remainder of the catheter can be considerably larger than the guide wire. Finally the guide wire is removed and the catheter remains and can be advanced to any desired distance. The technique is much simpler to perform than may appear from the description, and causes little discomfort to the patient.

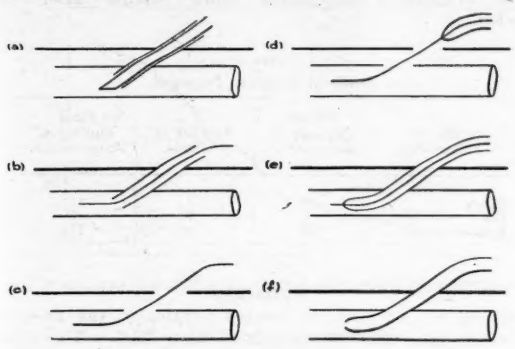

FIGURE I.

Diagram to illustrate the Seldinger technique of percutaneous catheterization of a vein. (*a*) Puncture of the vein with the cannula and needle. (*b*) The needle is removed, and a flexible guide wire is passed into the vein through the cannula. (*c*) The cannula is removed, the guide wire being left in the vein. (*d*) A tapered "Polythene" catheter is threaded onto the guide wire. (*e*) The catheter is advanced into the vein over the guide wire. (*f*) The guide wire is removed, the catheter being left in the vein. The catheter can be of larger size than the introducing needle, and there is no leakage at the puncture site.

Reports of Cases.

Three cases will be described briefly to illustrate the use of the method.

CASE I.—A woman, aged 41 years, received a massive transfusion (6·5 litres) of Rh-incompatible blood, after a severe post-partum hæmorrhage. Oliguric renal failure developed, and she was transferred to the unit on the fifth day of anuria. Oral feeding with hypertonic glucose solution had been poorly tolerated, and she was vomiting and mentally confused. A previous bilateral high ligation and stripping operation for varicose veins had been performed. A "Polythene" catheter was introduced percutaneously into the femoral vein by the Seldinger technique and advanced into the inferior vena cava. Glucose (500 ml. of a 50% solution per day) with added alcohol and heparin was administered. Despite a diuresis after 13 days of anuria, she continued to be intolerant of oral feeding, and the catheter remained *in situ* for a total of 12 days, with no complications. During this time she required one dialysis with the artificial kidney, with a Seldinger catheter introduced into the radial artery for the carriage of blood to the machine. She eventually made a complete recovery.

CASE II.—A woman, aged 69 years, developed renal failure after receiving an overdose of "Ansolysen" for severe hypertension. At the time of her transfer to the unit on the fifth day she was moribund and grossly overhydrated. Immediate dialysis produced a remission, and the following day a "Polythene" catheter was passed percutaneously into the superior vena cava through the median cubital vein by the Seldinger technique. She remained anuric and her condition deteriorated slowly; but the control of fluid and electrolyte balance was simplified by continued parenteral feeding. Renal biopsy confirmed the presence of chronic renal disease, and death occurred on the nineteenth day of anuria. There were no clinical complications from the caval infusion over the 14 days. An autopsy could not be obtained.

CASE III.—A woman, aged 32 years, developed acute renal failure after a self-induced septic abortion (*Clostridium welchii*). She was extremely ill when transferred to the unit on the fifteenth day of anuria, and an extensive sacral pressure sore was present. Immediate dialysis resulted in clinical and biochemical improvement. On the following day a "Polythene" catheter was inserted percutaneously into the inferior vena cava by the Seldinger technique via the opposite femoral vein to that employed for dialysis. Diuresis began on the nineteenth day, and the catheter was removed on the twenty-first day, when oral feedings were commenced. There were no complications from the catheter during the five days it remained in place, and the subsequent convalescence was uneventful.

Comment.

In each of the three cases described, the greater ease of medical and nursing care after the institution of parenteral therapy was striking. Vomiting and nausea were reduced, and the strain placed on the patient by treatment was considerably less.

The percutaneous introduction of the catheter by this technique was well tolerated by the patients, and in one case the absence of the saphenous veins would have rendered an open technique difficult.

Summary.

Patients with acute renal failure may be unable to take feedings orally, and parenteral therapy will on occasion be required.

As a high caloric intake in a minimum of fluid is desirable, concentrated solutions must be used, which require administration into a large central vein. The two main risks of this procedure are thromboembolism and infection, and the technique is justifiable only when strict care in their prevention is taken.

In this regard, the Seldinger technique of percutaneous introduction of a "Polythene" catheter offers certain advantages over other methods. The technique is applicable for administration into the superior or inferior vena cava, is readily mastered and causes little discomfort to the patient.

Three case histories are given to illustrate the usefulness of the method.

Acknowledgements.

I am grateful to Professor R. R. H. Lovell and Dr. A. E. Doyle, of the Department of Medicine, for permission to publish details of these cases. The cooperation and helpful advice given by Dr. H. A. Luke, Director of the Department of Diagnostic Radiology, Alfred Hospital, have been greatly appreciated. Professor M. R. Ewing has offered much valuable advice and criticism in the preparation of this paper.

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AMPUTATIONS FOR GANGRENE IN DIABETICS.

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It has been accepted that many factors contribute to gangrene in diabetics. Various authorities have stressed the importance of the vascular, the diabetic and the infective elements in ætiology, and therefore in treatment. Recently, stress has been laid on the value of purely local measures, and wide drainage and careful sequestrectomy have been pursued in spite of the ætiology.

During the years 1951 to 1955 inclusive, 62 diabetic patients were treated surgically at the Royal Prince Alfred Hospital for gangrene of some portion of a lower limb. This review has been based on the case histories and the follow-up investigation of these patients.

Attention has been paid to the age, sex and site incidence of gangrene, and to its duration. In addition, possible ætiological factors — for example, trauma, sensory disturbance or vascular deficiency — have been sought. An attempt has been made to relate the quantity and the quality of survival to the type of surgery employed in each case.

Clinical Findings.

The average age incidence was 66 years. Females outnumbered males in the ratio 2:1.

The duration of gangrene was variable, ranging from five days to 15 months. The average was nine weeks. The period in hospital averaged 32 days.

Sensory changes were recorded so infrequently that their relationship to other findings was doubtful.

In most cases trauma was not an obvious factor in the onset of gangrene; it was recorded as having occurred in 30% of cases.

The influence of infection was difficult to assess from the case records. Routine bacteriological examinations were not made, although in 50% of cases the clinical description implied the presence of gross infection.

The vasculature was examined usually at three sites — groin, knee, and ankle. Pulses recorded as "doubtful" have been regarded here as absent. Major vascular obstruction has been presumed to exist in the limb segment immediately beyond the most distal pulse. By clinical means, arterial obstruction was shown to exist in the thigh in 60% of patients, in the leg in 25%, and in the foot in 15%. Gangrene was usually in the toes, however, so that thrombosis of the digital vessels had evidently occurred as well.

Management.

These 62 patients were treated by several surgeons whose criteria of therapy were variable. No specialized diagnostic methods were used. The most common operation performed was mid-thigh amputation. Of the lower amputations, the great majority were local in the foot. Such procedures restricted to the foot included both classical amputations of toes or forefoot and purely "toilet" measures — *débridement*, sequestrectomy and drainage.

An attempt to control other factors was made in all cases, by the use of antibiotics and by stabilization of the diabetes.

Surgical Results.

The results of operation are set out in Table I.

Four of the original thigh amputations required further surgery to achieve healing. This comprised trimming of flaps or bone, removal of sloughs and resuturing.

Of the 22 amputations performed below the knee, 10 stumps failed to heal. All of these were in limbs with no pulses distal to the groin. The 12 successful "low" amputations were performed in limbs with definite pulses at knee or ankle.

Twelve of the original thigh amputations, however, were performed in limbs with pulses definitely discernible at the knee. In the light of previous findings, these amputations were too radical.

Sympathetic blockade of some type was carried out in seven cases before other surgery. In none was there any definite improvement, and in five instances the clinical state evidently deteriorated more rapidly after the blockade.

Table I.
Results of Operations Performed.

Site of Amputation.	Original Number of Amputations.	Number of Failures.	Final Number of Amputations.
Thigh	40	4	54
Leg	2	1	1
Foot	20	9	11

Mortality.

Among the 62 patients treated surgically, the five-year survival rate was slightly less than 25%. The great majority of deaths, both in and out of hospital, resulted from those diseases common to the age group — from cardio-vascular and respiratory diseases. No patients died from diabetes *per se*.

Both the hospital deaths described as "surgical" resulted from overwhelming infection, evidently stemming from the operation site. One was a clostridial infection; the other was not specified.

The details may be summarized as follows:

Hospital deaths: 10 (8 from respiratory or cardio-vascular diseases, 2 "surgical" deaths).

Patients discharged well, 52: 37 died of respiratory or cardio-vascular diseases; 11 were still living in August, 1959; 4 are presumably still living.

Functional Results.

All but four of the 62 patients have been traced. *Questionnaires* were forwarded, which sought information concerning the general state of health, the condition of the amputation stump, the circulatory state of the other limb and the degree of functional activity retained. Answers were received from the survivors, or from relatives or friends of the deceased, in 19 instances.

It was clear that about half of all the amputees had been converted by operation to a state of complete and permanent incapacity. Of the remainder, five only had been able to resume a normal degree of independence.

The 37 patients who died after leaving hospital survived for an average of two and a half years after operation (Figure 1). Three lived for more than five years. This small group consisted of patients whose disease allowed conservative surgery with ready healing, and in whom no other surgery on either limb was required at any time. Their early and continued mobility was therefore to be expected.

Discussion.

This review does not presume to analyse all the factors concerned.

The deficiencies in the routine case records were considerable, and the conclusions drawn, therefore, are gross.

It has been an inescapable conclusion that the vascular state is an outstanding factor in the choice of surgical treatment.

If there is popliteal pulsation, the limb deserves conservative surgery in the first instance; 40% of this series fell into this category. The patient's mobility should not be sacrificed for the surgical convenience of an unneces-

sarily radical amputation. Moreover, major surgery in these elderly patients carries a 15% mortality and a depressingly high morbidity. Their average stay in hospital alone exceeded one month.

If the popliteal pulse is not palpable, conservative surgery has been shown to have but a small chance of success.

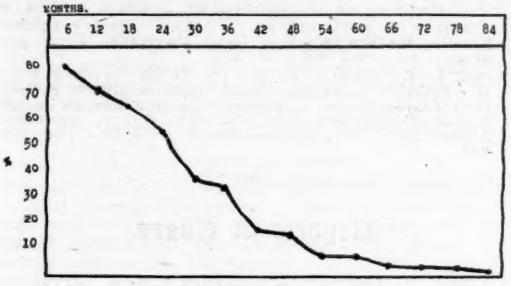

FIGURE I.
Percentage of patients surviving at varying periods post-operatively.

Acknowledgements.

I am indebted to Professor John Loewenthal for a great deal of advice in the preparation of this material, and to Miss M. Duncan, of the Department of Surgery, University of Sydney, for her care and assistance in the follow-up investigation of the patients reviewed.

PENICILLIN V BLOOD LEVELS AFTER ORAL ADMINISTRATION OF THE BENZATHINE AND HYDRABAMINE SALTS.

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AND
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From the Commonwealth Serum Laboratories, Melbourne.

RECENT investigations in humans on the absorption of oral preparations of penicillin V indicate that both the solubility and acid stability of its salts are important factors in the height of the serum concentrations obtained. A comparison of the solubilities of the commonly used preparations of penicillin V shows that the potassium salt is the most soluble, followed by the calcium salt, the free acid and the benzathine salt in that order, while the hydrabamine salt is the least soluble. When the relatively insoluble benzathine salt of penicillin V is administered orally, it is absorbed in sufficient quantities to give blood levels which are therapeutically useful. However, these levels are generally lower than those given by the soluble potassium penicillin V (Colquhoun *et alii, 1957; Juncher and Raaschou, 1957)* or by the less soluble free acid form (Putnam *et alii*, 1956; Brante *et alii*, 1958). Despite the widespread usage of hydrabamine penicillin V, which is less soluble than benzathine penicillin V, we have been unable to find any reports of the blood levels obtainable with the former salt.

Although it has been established that a rapid rate of solution is a desirable attribute for the rapid absorption of penicillin salts when given by the oral route (Nelson and Schaldemose, 1959), a slow rate of solution is advantageous, as it suppresses the unpleasant taste which is experienced when penicillin is swallowed in the form of either an oily or an aqueous suspension. In the case of an aqueous suspension, low solubility is also desirable in order to promote greater stability of the penicillin during storage. The degree of stability on storage over several months of an aqueous suspension of benzathine penicillin V containing suitable flavouring agents is at present unknown. This study was made in order to determine whether the hydrabamine salt of penicillin V offers any clinical advantage over the benzathine salt when judged by the concentration of penicillin obtained in the blood.

Materials and Methods.

The subjects were nine convalescent male patients at the Fairfield Hospital, whose ages ranged from 13 to 50 years. No patient had any known kidney disorder.

The oily suspension of the benzathine salt of penicillin V was prepared as a suspension in peanut oil, with ascorbic acid, oil of sweet orange and other flavouring agents added. The aqueous suspension was prepared in pineapple syrup together with other flavouring and suspending agents. The hydrabamine salt of penicillin V was administered as a commercially available banana-flavoured aqueous suspension. In each case the dose administered was equivalent to 250 mg. of phenoxymethylpenicillinic acid (approximately 400,000 units) contained in 2 dr. of suspension. The doses were given from 15 to 75 minutes after breakfast. The experiments were arranged as a set of three 3 by 3 Latin squares, each preparation being tested in three subjects on each of three days, as shown in Table I. The samples of blood were taken by venepuncture, one, two, four and six hours after the dose was administered. As soon as practicable after the blood had clotted, the serum was separated and refrigerated until the assays were performed. When the assays could not be made in the same day, the serum samples were stored at −20° C. The assays were made against a standard preparation of penicillin V, using fish spine beads on plates inoculated with *Sarcina lutea* (strain 9341 of the American Type Culture Collection). The standards, and the samples when necessary, were diluted with normal human serum. A preliminary sample of serum from each subject was demonstrated to contain no substances which would inhibit *S. lutea* by the technique described.

TABLE I.
Concentration of Penicillin V (in Units per Millilitre) in Serum at Various Intervals after an Oral Dose of 400,000 Units.

Subject Number.	Date of Test: January, 1960. Preparation.			Preparation A. Aqueous Suspension of Hydrabamine Penicillin V.				Preparation B. Aqueous Suspension of Benzathine Penicillin V.				Preparation C. Oily Suspension of Benzathine Penicillin V.			
	A.	B.	C.	1 Hour.	2 Hours.	4 Hours.	6 Hours.	1 Hour.	2 Hours.	4 Hours.	6 Hours.	1 Hour.	2 Hours.	4 Hours.	6 Hours.
1	20	15	12	0·7	2·2	0·5	0·2	2·7	5·4	0·5	0·1	0·5	0·3	1·9	0·5
2	15	12	20	4·1	2·4	0·3	0·07	4·6	2·2	0·9	0·3	0·7	0·9	0·9	0·2
3	12	20	15	1·5	0·9	0·2	0·03	0·5	0·7	0·5	0·5	0·3	0·2	1·4	0·3
4	—	12	15	—	—	—	—	2·4	1·5	0·5	0·05	0·2	0·2	1·5	0·3
5	15	20	12	2·2	1·4	0·2	0·07	1·7	2·4	0·5	0·2	0·5	0·7	0·3	0·05
6	12	15	20	5·8	0·7	0·1	0·05	3·4	1·9	0·14	0·03	1·4	1·0	0·09	0·07
7	12	15	20	5·8	4·1	0·5	0·1	2·9	1·0	0·5	Sample lost	1·9	0·9	0·5	0·2
8	15	20	12	2·9	1·9	0·2	0·03	1·4	1·9	0·7	0·2	2·0	0·5	0·9	0·2
9	20	12	15	0·9	1·4	0·3	No sample	1·7	1·5	0·5	0·09	0·9	2·4	0·3	0·07
Median				2·6	1·7	0·3	0·07	2·4	1·9	0·5	0·15	0·7	0·7	0·9	0·2
Arithmetic mean				2·98	1·85	0·29	0·07	2·36	2·06	0·53	0·19	0·92	0·78	0·87	0·22

Results.

The concentrations found in the sera one, two, four and six hours after the dose had been administered are shown in Table I, and the arithmetic mean concentrations for each preparation in Figure I. The concentrations of penicillin found at one and two hours after the administration of the oily preparation of benzathine penicillin V were significantly lower than those at the corresponding times after the aqueous preparations ($P < 0.05$). On the other hand, the concentrations found at four and six hours after the administration of benzathine penicillin V were significantly higher than those at the corresponding times after the aqueous suspension of hydrabamine penicillin V ($P < 0.05$).

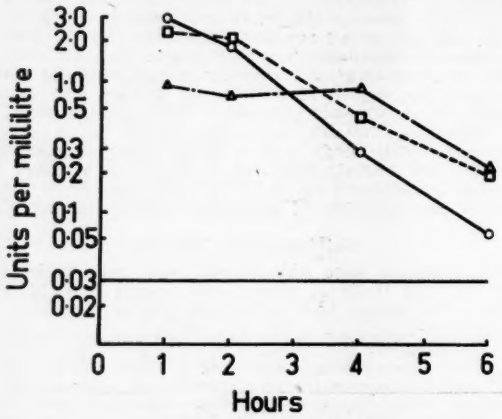

FIGURE I.

Mean concentrations of penicillin found in serum after oral administration of 400,000 units of penicillin V as hydrabamine salt (aqueous suspension, solid line and circles), or as benzathine salt (aqueous suspension, interrupted line and squares, or oily suspension, broken line and triangles).

Discussion.

Although this trial was made on a small scale, it confirmed earlier reports that doses of benzathine pencillin V corresponding to the routine doses of other salts of penicillin V give therapeutically useful concentrations of penicillin in the serum for at least six hours. It was clearly shown also that the hydrabamine salt gives satisfactory concentrations of penicillin in the serum, but offers no advantage over the benzathine salt when serum levels alone are considered. Incorporation of the benzathine salt in an oily vehicle appears to delay the absorption when compared with an aqueous vehicle, but this disadvantage is offset by the persistence of higher blood levels at four to six hours.

Summary.

1. Nine convalescent males were given after breakfast 400,000 units of an aqueous suspension of hydrabamine penicillin V and of aqueous and oily suspensions of benzathine penicillin V. Penicillin was determined in samples of serum taken one, two, four and six hours after the dose.

2. All the preparations maintained therapeutically useful serum levels for at least six hours.

3. At one and two hours after the dose, the serum levels were significantly higher with the aqueous suspensions than with the oily suspension. At four and six hours the levels were significantly higher with the benzathine than with the hydrabamine salt.

Acknowledgements.

Our thanks are extended to Dr. H. McLorinan and the staff and patients of Fairfield Hospital for their cooperation in making this trial possible. We also wish to thank Mr. W. Bousfield for conduct of the assays.

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Reports of Cases.

TUBAL PREGNANCY ASSOCIATED WITH TUBERCULOUS SALPINGITIS.

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BOTH tuberculous salpingitis and tubal pregnancy are quite commonly seen in gynæcology and pathology departments, but the combination of the two would appear to be extremely rare. Davin-Power, O'Dwyer and Leslie (1955) reported a case which they believed to be only the fifty-third recorded instance, and only the third published in the British literature. Since then at least five more cases have been added, including one by Peretz (1958) of recurrent ectopic pregnancy with tuberculous salpingitis. In a series of 313 ectopic pregnancies and 197 cases of tuberculous salpingitis, extending over a period of 54 years, Kistner, Hertig and Rock (1951) only once found the dual condition. The following case is considered worth reporting.

Clinical Record.

Mrs. W., aged 24 years, was admitted to the Royal Hobart Hospital on May 11, 1959. The patient had been married for five years, and though desiring a family, had had no children or miscarriages. Her mother had died of tuberculosis nine years before. The patient's menstrual periods had followed a 28-day cycle, lasting for six days. The last normal menstrual period had occurred on March 28. On her admission, to hospital the patient said that 10 days before she had contracted a respiratory tract infection with cough and sore throat. It had lasted for about three days, and been followed by pain in the back and in the lower part of the abdomen, scalding on micturition, and a loss of dark blood per vaginam. Two days before her admission to hospital the abdomen had become swollen and tense, and there was pain on movement.

Examination of the patient revealed some guarding and tenderness of the abdomen, most marked in the left iliac fossa. There was a small mass of tissue being extruded from the cervix, and blood was present in the vagina. Bimanual exmination disclosed a normal-sized uterus. Palpation of the uterus demonstrated extreme tenderness, particularly on the left side. The respiratory and circulatory systems were normal.

A provisional diagnosis of ectopic pregnancy was made, and laparotomy was performed. Operation disclosed a left tubal abortion with about a litre of free blood and blood clot. Both Fallopian tubes varied considerably in diameter along their length, and the fimbrial end of the right tube was closed by adhesions. The ovaries appeared normal. The left tube was removed and placed in formalin.

The patient had an uneventful convalescence. In view of the pathological report, she was given streptomycin, P.A.S. and I.N.A.H. A chest X-ray examination showed calcified lesions, considered to be tuberculous, at the apex and hilum of the left lung. No tubercle bacilli were found in the sputum.

Pathological Examination.

Macroscopic Appearance.

The specimen consisted of a Fallopian tube, which was swollen, distorted and discoloured at the fimbrial end, with a loosely attached mass of blood clot measuring 4 by 3 cm. The appearances indicated a tubal abortion.

Microscopic Appearance.

The clot attached to the tube contained chorionic tissue. The tubal mucosa was generally adenomatous, some areas being fairly normal, but most showing numerous collections of endotheloid and giant cells considered to be typically tuberculous. No caseation was evident. Numerous lymphocytes, plasma cells and polymorphs infiltrated the submucous tissues. In addition, there were foreign-body giant cells, some of which contained anisotropic crystals soluble in normal hydrochloric acid (Figure I).[1] Schaumann bodies were prominent in some areas. These were generally rounded, and though most showed no definite pattern, some had typical lamination (Figure II). No anisotropic material was seen in the Schaumann bodies. Several areas of the tube were hæmorrhagic, and a few of the stromal cells showed a decidual change. The tissue removed from the cervix was a decidual cast. No tubercle bacilli could be demonstrated by Ziehl-Neelsen staining.

Comment.

In the absence of demonstrable tubercle bacilli, a diagnosis of tuberculous salpingitis cannot be certain. However, the difficulty of finding tubercle bacilli is well known. The presence of Schaumann bodies is regarded by Burne (1953) as being virtually diagnostic of old or recent tuberculous salpingitis. Anisotropic crystals are also typical of this condition, and according to Berenbaum and Korn (1954) they consist mainly of calcium carbonate. As the crystals in this case dissolved in hydrochloric acid, talc granuloma is excluded. Other points in favour of the diagnosis are the X-ray appearances in the lung and the family history of tuberculosis. Views advanced for the rarity of pregnancy occurring in a tuberculous Fallopian tube are obstruction to the patency of the tube, and the diseased mucosa, in which nidation is unlikely to occur.

Summary.

1. A case of ectopic gestation occurring in a tuberculous Fallopian tube is described.

2. Tubercle bacilli were not found; but the general appearance, including anisotropic crystals and Schaumann bodies, is strongly in favour of a diagnosis of tuberculous salpingitis.

Acknowledgements.

We are indebted to Dr. J. Edis and to Dr. P. Nolan, General Superintendent, Royal Hobart Hospital, for permission to publish this case.

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[1] For Figures I and II see art-paper supplement.

ANEURYSM OF THE RIGHT PULMONARY ARTERY IN A PATIENT WITH ATRIAL SEPTAL DEFECT CAUSING RIGHT MIDDLE-LOBE COLLAPSE.

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AND
IAN H. MCCONCHIE, M.S., F.R.A.C.S.,
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ANEURYSMS of the pulmonary artery have been described previously (Reid, *et alii*, 1959). Aneurysms in peripheral pulmonary arteries are not uncommon. They may be associated with infected pulmonary emboli, or they may be caused by external erosion when they are in the wall of a tuberculous cavity.

Aneurysms of the main pulmonary artery and major branches are uncommon. In reviews of this condition (Blades *et alii*, 1950; Boyd *et alii*, 1939; Deterling *et alii*, 1947) covering a total of 147 cases, 30% of the cases were attributed to syphilis. With the general decline in venereal infection, this figure is certainly too high now. Congenital heart disease with a left-to-right shunt and increased pulmonary blood flow was next in frequency. Mycotic and traumatic aneurysms were rare.

Aneurysms may rupture or thrombose. In addition, because of their size, they may cause symptoms by pressure on surrounding structures. The present patient is of particular interest because she presented with such a complication. The aneurysmal right pulmonary artery, compressing the right bronchus intermedius, caused right middle-lobe collapse. Atrial septal defect was diagnosed on clinical examination. The diagnosis was subsequently confirmed by cardiac catheterization, and the defect was later treated surgically.

Clinical Record.

Mrs. A., aged 40 years in 1959, was referred from the mass X-ray surveys because the X-ray film of her chest suggested collapse of the middle lobe of the right lung (Figures IA and IB).[1] Eight weeks prior to the X-ray examination, the patient had suffered an attack of influenza with cough and sputum. These symptoms had persisted until the time of the X-ray examination. For some years she had noticed shortness of breath on moderate exertion, and more recently she had been short of breath when she hurried on the flat. She had never noticed swelling of the ankles. She had frequent attacks of purulent bronchitis, and she had had an hæmoptysis two years previoulsy. There was no past history of rheumatic fever, nor had the patient's heart ever been questioned on routine examination.

On clinical examination of the patient there was evidence of collapse of the middle lobe of the right lung, and the examination of her cardio-vascular system strongly suggested the presence of an atrial septal defect. The pulse was regular and of normal volume. The blood pressure was 115/80 mm. of mercury. The jugular venous pressure was not elevated, but the *a* wave was dominant over the *v* wave. There was no evidence of heart failure. On palpation of the precordium, there was a lift both over the pulmonary artery and at the lower left sternal edge, typical of a hyperdynamic right ventricle. On auscultation, there was an ejection-type systolic murmur, Grade 2 out of 6, heard at the pulmonary area, followed by a widely split second sound. The two components of the second sound were split by 0·08 of a second. Pulmonary valve closure was accentuated and did not move during respiration with relation to aortic valve closure (Leatham *et alii*, 1956). At the left sternal edge there was an early systolic ejection sound, which increased in intensity during expiration. The first sound was clearly split at

[1] For Figures IA, IB, IIIA, IIIB, and V see art-paper supplement.

the mitral area (Figure II). The electrocardiogram demonstrated an abnormal *P* wave with a prolonged *P-R* interval of 0·24 second (Zuckermann *et alii*, 1951). Right axis deviation and right ventricular hypertrophy were present. An X-ray film of the chest confirmed the presence of collapse of the middle lobe of the right lung without evidence of other pulmonary disease. The heart was considerably enlarged (cardio-thoracic ratio 17 to 27 cm.). The right pulmonary artery was aneurysmal. The lung fields were plethoric, and fluoroscopic screening revealed marked hilar dance, with a particularly prominent pulsation in the right pulmonary artery shadow.

With postural coughing and breathing exercises, the right middle lobe partly reexpanded. A bronchogram showed some residual collapse in that lobe, and in addition it demonstrated compression of the right bronchus intermedius by the aneurysmal right pulmonary artery (Figures IIIA and IIIB).

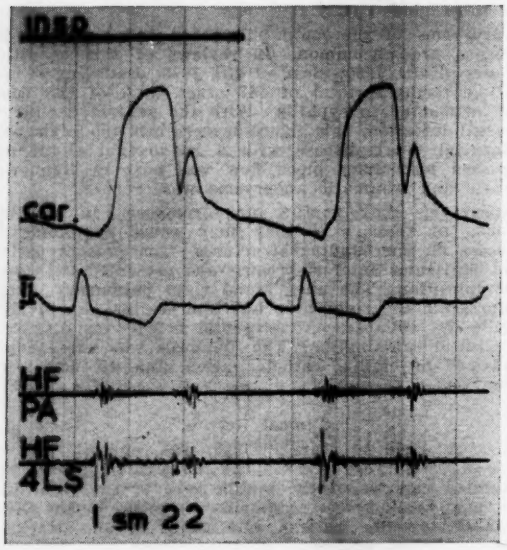

FIGURE II.

Pre-operative phonocardiogram. The aortic and pulmonary components of the second sound were split by 0·08 second and were fixed during respiration. The ejection sound occurred 0·04 second after the onset of the first sound.

After further physiotherapy and chemotherapy catheterization of the right side of the heart was carried out, and this confirmed the diagnosis of an atrial septal defect. The pulmonary to systemic flow ratio was 3·2 to 1·0. The pulmonary artery pressure was 35/18 mm. of mercury. The catheter was passed through the atrial septal defect into the left atrium and into the left ventricle. The position of the catheter with the tip in the left ventricle suggested a secundum type of atrial septal defect.

Bronchoscopy was performed by Dr. Brian Marks. The right main and intermediate bronchi were displaced backwards, and their anterior wall was seen to be bulging inwards and pulsating. The overlying mucosa was normal. No excessive secretion was seen. It was concluded that displacement and compression of the right main and intermediate bronchi by the aneurysmal right pulmonary artery could be the cause of the right middle-lobe collapse.

The atrial septal defect was closed under vision by direct suture, with the use of moderate hypothermia at 30° C. and inflow occlusion for seven minutes. The defect measured 4 by 2 cm. and was situated in the region of the foramen ovale. The mitral and tricuspid valves were normal. It was confirmed that the right pulmonary artery was aneurysmal where it lay in close proximity to the right bronchial tree. It was noted that the medial segment of the right middle lobe was collapsed.

The patient made an uneventful recovery after operation. The systolic murmur disappeared, and after about one week the two components of the second sound moved normally during quiet respiration. The early systolic ejection sound remained as an indication of the dilated main pulmonary artery. It could be heard loudly at the base of the heart and left sternal edge (Figure IV). The post-operative chest X-ray films showed much less pulmonary plethora without any evidence of right middle-lobe disease. The heart had decreased in size (Figure V).

Discussion.

Pulmonary artery aneurysms carry a poor prognosis. Sudden death may be caused by rupture. Blades *et alii* (1950) reported that about one-third of such aneurysms caused death by rupture. Therefore, surgery should be considered in the management of this condition. If there is a causal congenital heart defect, then this should be investigated and treated if possible. Repair of the atrial septal defect in our case reduced the size of the aneurysmal dilatation of the pulmonary artery and removed the pressure from the right bronchus intermedius. Danger of rupture was correspondingly reduced, and we hope the patient will have fewer attacks of purulent bronchitis and no further episodes of right middle-lobe collapse or infection. If a direct attack on such an aneurysm was contemplated, angiocardiography would be a useful pre-operative investigation.

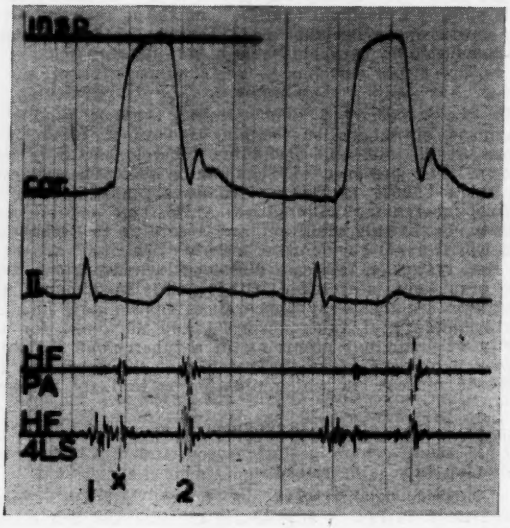

FIGURE IV.

Post-operative phonocardiogram. The two components of the second sound move normally during respiration. The early systolic ejection sound remains.

Summary.

An unusual complication of an aneurysmal right pulmonary artery in a patient with an atrial septal defect is described.

Surgical repair of the atrial septal defect was carried out, and the patient has subsequently remained free of pulmonary symptoms.

Acknowledgements.

We wish to thank Dr. C. H. Fitts for referring this patient. Dr. Brian Marks carried out the bronchoscopic examination. Hypothermia and anæsthesia were managed by Dr. T. Currie. Mr. George Westlake assisted at the

operation. The illustrations were prepared by Mr. Ingles.

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INFANTILE PYKNOCYTOSIS OCCURRING IN DISSIMILAR TWINS.

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TUFFY *et alii* (1959) recently described for the first time a self-limiting hæmolytic anæmia which developed during the first three months of life, and which was characterized, at the morphological level, by a significant increase in the number of pyknocytes in the blood film. They defined pyknocytes as much distorted, completely irregular erythrocytes, usually smaller than the accompanying normal red blood cells and having several to many spiny projections. These cells stain more intensely than normal cells, and in this feature resemble spherocytes. The authors pointed out that similar cells might be found in the blood of healthy full-term infants (range 0·3% to 1·9%) and in premature infants (range 1·3% to 5·6%), the higher level appearing in the older infants aged up to three months. The presence of pyknocytes to the levels stated appeared to be within normal range, and was not associated with any undue rapidity of red blood cell destruction. As the result of the study of 11 affected infants, the authors concluded that pyknocytes were likely to be found to levels of 50% of all red blood cells. Heinz bodies were not a feature. The liver and spleen were usually enlarged and there was mild jaundice. The disease was transient and responded to supportive therapy.

Two cases of this disease, occurring in dissimilar twins, have now been recognized in this hospital, and reports of these two cases follow.

Family History.

Both parents are of British stock and are third generation Australians; the parents are not consanguineous. This was the second gestation. The first resulted in a stillbirth at seven months, approximately 12 months before the birth of twins, death in utero then being diagnosed at 24 weeks; the cause of death could not be determined. There were no unusual features noted during this gestation, and close questioning failed to reveal any exposure to drugs or chemicals. Investigation of the family history revealed that on the father's side two siblings out of six had been jaundiced early in infancy; their mother was Rh-negative, and no antibodies were ever found. The grandfather had also been jaundiced early in infancy. All the members of the family have been in good health since. There was no relevant information on the maternal side of the family.

Clinical Record.

A., a female child, aged one month, was admitted to the Royal Alexandra Hospital for Children because of progressive jaundice and pallor of three days' duration. She was the first born of dissimilar twins, delivered approximately three weeks prematurely, weighing 5 lb. 7 oz. Jaundice was noted on the fifth day, when investigations made elsewhere revealed a serum bilirubin content of 9 mg. per 100 ml. The hæmoglobin value was 17·1 grammes per 100 ml., and examination of the blood film was reported as showing normal leucocytes, and no spherocytes or any other evidence of hæmolytic anæmia. The serum bilirubin level had fallen to 5·5 mg. per 100 ml. by the following day. By the fourteenth day the hæmoglobin value had fallen to 12·3 grammes per 100 ml., when the blood film appearances were again reported as normal. The child was then discharged from the maternity hospital, and her progress was said to have been satisfactory until three days prior to the present admission. Investigations made elsewhere on the day of her admission to this hospital were reported as giving the following results: hæmoglobin value, 5·5 grammes per 100 ml.; red blood cell count, 1,100,000 per cubic millimetre; white cell count, 12,500 per cubic millimetre (28% neutrophils, 1% eosinophils, 60% lymphocytes, 8% monocytes and 3% metamyelocytes). The comment on the blood film was that the red blood cells showed marked variation in size and shape with polychromasia. No spherocytes were seen. The serum bilirubin content was 2·0 mg. per 100 ml.

The second born twin, a boy, B., had been delivered by the breech, and his birth weight was 5 lb. 4 oz. He failed to thrive for some time, and was kept in the maternity hospital until the age of one month. The only investigation was made on the fourteenth day, when a blood examination showed the hæmoglobin value to be 17·7 grammes per 100 ml. and the red blood cells to number 5,500,000 per cubic millimetre; the blood film was commented upon as normal. Since the child's discharge from the maternity hospital he had seemed to progress satisfactorily.

Examination of the first twin, A., on her admission to hospital showed her to be an active baby, apyrexial, jaundiced and pale. Both spleen and liver were slightly enlarged. There were no other abnormal clinical findings. The hæmoglobin value was 5·7 grammes per 100 ml. Of the red blood cells, 10% were reticulocytes. A blood film showed marked anisocytosis with occasional coarsely stippled cells. Approximately 20% of the red blood cells showed pyknocytic features — they were distorted and irregular and stained intensely, many having several spiny projections resembling spiny spherocytes (Figure I). Thrombocytes were numerous. The Coombs tests (direct and indirect) and the papain-sensitized red blood cell test for the detection of incomplete antibodies gave negative results. Results of a urine examination were normal. At this stage the diagnosis of hæmolytic anæmia of unknown ætiology was made. A transfusion of 120 ml. of whole blood was given immediately, and the next day the hæmoglobin value was 11·2 grammes per 100 ml., the red blood cells numbered 4,000,000 per cubic millimetre and the colour index was 0·9. Of the red blood cells, 14% were reticulocytes; the white cell count was 10,000 per cubic millimetre (57% neutrophils, 40% lymphocytes, 3% eosinophils). There were 600 nucleated red blood cells per cubic millimetre. Thrombocytes were numerous. No Heinz bodies were detected. The film showed marked polychromasia and anisocytosis, and about 20% pyknocytes. During the next few days the jaundice faded and the spleen and liver decreased in size. On the sixth day after the child's admission to hospital the hæmoglobin value was 12·8 grammes per 100 ml., 4% of the red blood cells were reticulocytes and approximately 20% of cells were pyknocytes.

The parents were then examined. All hæmatological investigations, including estimations of fragility and autohæmolysis (with and without glucose), gave normal results.

The patient was then discharged from hospital, and subsequently examined at the follow-up clinic at the age of seven weeks. Her colour was good, she was active and there was no jaundice; the liver and spleen were not enlarged. The hæmoglobin value was 11·0 grammes per 100 ml., the red blood cells numbered 3,600,000 per cubic millimetre, the colour index was 1·0, and 1·2% of the red blood cells were reticulocytes. Approximately 10% of the red blood cells were pyknocytes. The white cell count was normal, with a normal distribution.

Her twin brother was examined on the same day for the first time and he appeared an active healthy baby.

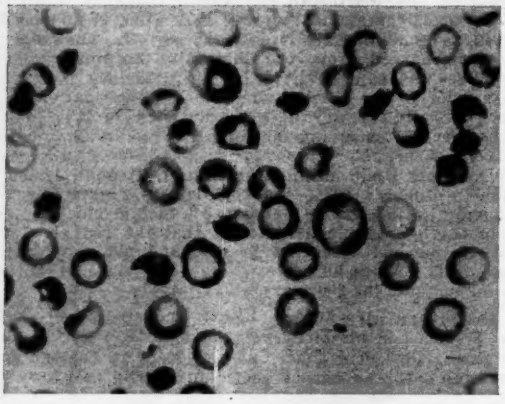

FIGURE I.

The hæmoglobin value was 8·4 grammes per 100 ml., the red blood cell count was 2,570,000 per cubic millimetre and the colour index was 1·1. Of the red blood cells, 7·2% were reticulocytes. The white cell count was 10,000 per cubic millimetre, and the distribution was normal. Approximately 10% of his red blood cells were pyknocytes (Figure II). Thrombocytes were numerous. No treatment was given.

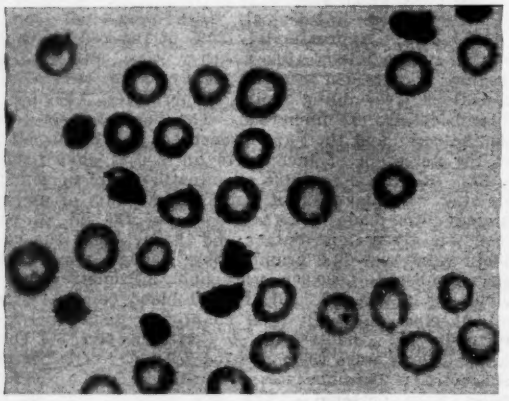

FIGURE II.

Both twins were again examined at the ages of 12 weeks and 16 weeks, and found to be healthy looking and without clinically detectable abnormalities; they had normal blood findings for their age. Only about 1% of red blood cells were pyknocytes.

Through the courtesy of the Red Cross Blood Transfusion Service in Sydney, further investigations of both parents and twins showed the mother's blood group to be O, Rh-positive (genotype CcDee), the father's B, Rh-negative (genotype ccddee), and that of both twins O, Rh-negative (genotype ccddee). No atypical antibodies were found. The mother's serum was compatible with both infants' red blood cells.

Discussion.

On both clinical and laboratory investigation the twins seem to coincide with the description of infantile pyknocytosis as given by Tuffey *et alii* (1959). The condition may closely resemble hæmolytic disease of the newborn; in this particular case this seems an unlikely possibility, in view of the stated blood group genotype of both parents and their twins.

One of the twins presented with a hæmolytic anæmia severe enough to warrant an immediate blood transfusion; in the other twin, anæmia associated with pyknocytosis was discovered by routine examination only, yet the infant seemed healthy. Both twins had approximately the same number of pyknocytes at the age of seven weeks. These facts, in association with a history of jaundice on the paternal side of the family without subsequent clinical illness, may possibly be significant in postulating a familial ætiological factor. If this was the case, then it would appear that the condition was transmitted as a Mendelian characteristic with various degrees of penetrance during infancy.

After a blood transfusion of approximately one-quarter of the infant's blood volume, the level of pyknocytes remained stationary for some time. A similar observation was made by Tuffy *et alii* in one of their cases; this would tend to confirm the original statement that an extracorpuscular mechanism affects some of the normal donor's red blood cells in such a way that they assume the pyknocytic form in the patient.

A comparison of morphological features on a stained smear from a case of acanthrocytosis on file at this hospital in the Institute of Pathology with the present case would indicate that in acanthrocytosis there are more abnormal cells (about 70%) present than in pyknocytosis, yet only a proportion of these crenated cells are dense and stain deeply, resembling contracted spherocytes with pseudopodia. In pyknocytosis, on the other hand, the abnormal cells on the whole tend to be more irregular, and almost all the abnormal cells are dense and stain intensely. This is in accord with the description of acanthrocytes as given by Basson *et alii* (1950), and as shown in the photomicrograph accompanying their report.

Summary.

A case of infantile pyknocytosis occurring in dissimilar twins is described.

In the first twin the condition presented as acute idiopathic hæmolytic anæmia, and remitted with supportive treatment by the age of three months. In the second twin the condition was discovered by routine examination only, eventuating in spontaneous remission at the same age as in the first twin.

Some relevant points concerning possible ætiological factors and differential diagnostic features have been stressed.

Acknowledgements.

I am grateful to Dr. R. D. K. Reye, Director of the Institute of Pathology, Royal Alexandra Hospital for Children, for his constructive criticism of this paper, and to Professor L. Dods, on whose patients this investigation was carried out. I should like to thank Dr. R. Walsh, Director of the Red Cross Blood Transfusion Service in Sydney, for the serological data.

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RECOVERY FROM OBSTETRIC SHOCK PROBABLY DUE TO AMNIOTIC FLUID EMBOLISM.

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WHEN Thomas De Quincey "by one flash of simultaneous intuition", had his vision of sudden death, he had the comfort of a physical explanation for his fear, even though enlivened by laudanum. But what comfort has a healthy young woman, who is suddenly afflicted with a malady she cannot understand, and intuitively knows that she is in the "Valley of the Shadows"? Her physician, whilst denying her premonition when she asks "Am I going to die, doctor?", must reassure her, quickly assess the cause, and not rest until, in retrospect, he can say with De Quincey, "all had been done that, by me, could be done; more on my part was not possible".

One of our young mothers passed through a similar harrowing experience late last year, when the initial diagnosis of pulmonary embolism due to blood clot was made and appropriate treatment instituted. After an X-ray examination of the chest on the third day after delivery, this was changed to amniotic fluid embolism (Lushbaugh's syndrome). Whilst the existence of this syndrome is denied by some, it has been widely recognized since it was first described by Steiner and Lushbaugh in 1941. Unfortunately, absolute proof of the diagnosis depends upon post-mortem findings, and when recovery occurs, as it occasionally does, the condition can be confused with several other clinical entities with similar symptoms, signs and radiological appearances. Thus the case described is similar to Lushbaugh's syndrome, and in all probability is an example of recovery from it.

Clinical Record.

In 1952, at the Royal North Shore Hospital of Sydney, Mrs. D., aged 18 years, was delivered of her first child by Cæsarean section, the indications being the presence of moderately severe toxæmia in a primipara in whom the ischial spines were prominent, although X-ray pelvimetry showed an adequate pelvis in all other respects. She had no further pregnancies until 1958, when she had an incomplete miscarriage, and her uterus was curetted on October 27.

In 1959 she became pregnant a third time and was due for confinement on November 4. The ante-natal period was normal until the middle of October, when she gained excess weight and developed mild hydramnios. Her total weight gain throughout the pregnancy was 25 lb., and her blood perssure remained under 130/70 mm. of mercury. The urine was free of albumin, and although her blood group was O, Rh-negative, the results of tests for anti-Rh agglutinins remained negative. The hydramnios was treated with rest, salt restriction and "Diamox". She was admitted to hospital in good health towards the end of October with the fœtal head engaged, the intention being to allow a trial of labour, and if dystocia occurred to perform another lower segment section.

At 10 p.m. on October 29 early labour commenced, and progressed normally without any undue distress to the patient. At about 5 p.m. on October 30, with the fœtal head on the perineum, a short "open ether" anæsthetic was given by my partner (atropine, 1/100 grain, being given by hypodermic injection as premedication), and the baby was delivered by forceps with great ease. The baby was a normal living female weighing 9 lb. The third stage was uneventful, and the placenta showed no obvious abnormality.

About half an hour after delivery the patient, now fully awake, complained of a severe pain in the chest just to the right of the lower part of the sternum, and became very shocked, distressed and dyspnœic, with cyanosis; with the fall in blood pressure, rise in pulse rate and nausea, she felt that she was going to die, and her appearance suggested that this might be the unhappy outcome. Later she was able to say that the pain in the chest first came on as she was going under the anæsthetic, but at the time she was unable to protest. Examination of the chest at this stage revealed a few crepitations at both lung bases. There was no post-partum hæmorrhage or evidence of rupture of the previous uterine scar to account for the state of shock, and in view of the chest pain, a diagnosis of pulmonary embolism was made.

Treatment was rapidly instituted—oxygen by the intranasal route, morphine (one quarter of a grain) and heparin given intravenously. Through an indwelling Mitchell needle 5000 units or more of heparin were injected every six hours, the dose being varied to maintain the coagulation time at 10 minutes or slightly longer. This was continued for six days, and at no time was there any excessive uterine bleeding. "Achromycin V" was given orally, one capsule every six hours, to prevent pulmonary infection. As the hæmoglobin value was satisfactory (12 grammes per 100 ml.), no unusual hæmorrhage was evident and pulmonary œdema could be anticipated, no transfusion of blood or other fluids was given.

After a few hours the patient developed a moist cough and brought up blood-stained sputum. Moist râles were audible now widely over both sides of the chest. Distension of the upper part of the abdomen became apparent next morning, but as no real tenseness occurred, it did not seem to worry her. X-ray examination of the chest was delayed until the third day, when she felt better and movement no longer upset her. The picture was one of widespread mottling in both lungs, and this led to the change of diagnosis to amniotic fluid embolism. As suggested by Weiner and Reid (1950), the heparin injections were continued. Clinical recovery was now rapid, so that by the ninth day the X-ray film of the chest was virtually clear and she was allowed to feed her baby. She was discharged from hospital, feeling well, on November 11, the twelfth day after confinement.

Discussion.

Seltzer and Schuman (1947) have recorded a case similar to the foregoing, and ascribe the recovery of their patient to the absence of anaphylaxis and uterine hæmorrhage. They state that "analyses of 72 obstetric deaths by Steiner and Lushbaugh (1941) showed that pulmonary emboli by amniotic fluid contents is the most common cause of death in the period during labour and within the first nine hours thereafter". Further, they list the physical findings common to the cases of Steiner and Lushbaugh and their own as follows: (a) sudden onset with shock; (*b*) cyanosis; (*c*) dyspnœa; (*d*) fall in blood pressure; (*e*) râles (pulmonary œdema).

The X-ray picture is illustrated in "British Obstetric and Gynæcological Practice" (Vol. I, first edition, page 815), and the appearance is described as "diffuse mottling such as seen in miliary tuberculosis". All these clinical findings were present in the above history, the only unusual symptom being the presence of chest pain, which was the initially predominant symptom; but according to Lewis (1956), pain in the chest is not a feature of Lushbaugh's syndrome.

The following other conditions can have a similar onset, with shock and an X-ray picture of the chest identical with that in the present case.

1. Bronchopneumonia of sudden onset with shock. However, the patient had no respiratory symptoms prior to the induction of anæsthesia, subsequently remained afebrile and recovered relatively rapidly. Antibiotic therapy would hardly have been adequate if this had been a case of severe infective bronchopneumonia.

2. Acute heart failure. There was no previous history of rheumatic or other heart disease, clinical examination of the heart revealed no abnormality, and an electrocardiogram on the fifth day was quite normal.

3. Regurgitation and inhalation of gastric contents. No vomiting or coughing occurred during the induction of anæsthesia, and on subsequent questioning, the patient, who remembered the onset of pain well, could not recall any burning sensation in her throat or any desire to vomit. Seltzer and Schuman state that atelectasis would be the more likely X-ray picture in this event; but Dr. Eric Frecker has advised that bronchopneumonia is consistent with the inhalation of gastric contents. As far as it is possible to ascertain, this did not occur, and the rapid recovery would hardly be expected if bronchopneumonia was due to this cause.

None of the above-mentioned conditions would be expected to give rise to severe post-partum hæmorrhage; nor did it occur in the case under discussion. However, amniotic fluid embolism is one of the syndromes associated with severe bleeding due to the incoagulability of blood. Mayes (1959) states that "in those cases who survive long enough after passage of amniotic fluid into the blood, severe post-partum hæmorrhage may occur due apparently to the coagulative effect of amniotic fluid on blood and the subsequent fibrinopenia". Lewis has drawn attention to several reports of cases treated successfully with fibrinogen.

Is this bleeding diathesis an essential element in the diagnosis of the amniotic fluid embolism syndrome, as has been maintained by some? Or is it a complication which occurs sometimes? The latter seems the better interpretation for the following reasons: (a) It was not considered an essential element by Lushbaugh. (b) It occurs in association with other obstetric disorders, such as the retained dead fœtus syndrome and, particularly, severe accidental hæmorrhage. Even in the latter condition, the occurrence is estimated at less than 5%. (c) The mechanism by which the blood becomes incoagulable is still subject to much research and speculation, and the following factors in the present case may have had some influence in avoiding the complication: absence of violent uterine contractions, often described in Lushbaugh's syndrome, and hence reduction in the amount of amniotic fluid injected into the blood vessels; absence from the amniotic fluid of any observable meconium; the early exhibition of heparin, which may have limited the degree of defibrination, and thus allowed time for the liver to restore any losses, as it normally does in four to five hours.

Summary.

1. A case of recovery from severe obstetric shock in a multipara who had had a previous Cæsarean section is presented.

2. The probable cause of the shock was amniotic fluid embolism.

3. Recovery is attributed to infusion of a sublethal dose of amniotic fluid free of meconium, with consequent reduction in the degree of anaphylactoid shock, and absence of severe post-partum hæmorrhage due to incoagulability of blood.

Acknowledgements.

I wish to thank the matron and staff of the Coonabarabran Hospital for their devoted nursing; Professor B. T. Mayes and Professor R. P. Shearman for their comments; and Dr. S. W. Wherrett and Dr. Eric Frecker for their advice on the X-ray films.

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THE DIABETIC STATE IN ACUTE PANCREATITIS: A CASE REPORT.

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A DISTURBANCE of carbohydrate metabolism is not an uncommon complication of acute pancreatitis, but an initial blood sugar level of 1500 mg. per 100 ml. is probably rare. For this reason the following clinical record has been reported.

In acute pancreatitis, abnormalities of glucose tolerance and hyperglycæmia are more common than glycosuria; but as a transient phenomenon none are rare, and they have been reported together in as many as 50% of cases (Dreiling and Janowitz, 1956). The presence of hyperglycæmia has also been estimated as 50% to 100% and of glycosuria as 5% to 26% by various authorities.

Some authors consider that the prognosis of acute pancreatitis is worse if it is complicated by abnormalities of carbohydrate metabolism. Pollock (1959) regards this complication, amongst other things, as serious, and in his analysis of 100 cases found 14 in which there was a high fasting blood sugar level or "diabetic" glucose tolerance curve; eight of these patients died, one probably from untreated diabetic coma. Warren, Fallis and Barron (1950), in their series of cases of acute pancreatitis, found 38 severely ill patients, and five of these had acute diabetes. Of these five, two died, and it is interesting to note that the highest blood sugar level recorded was 382 mg. per 100 ml. in this group. Other diabetic deaths are mentioned by Siler, Wulsin and Carter (1955), and also by Tourtellotte and Tyler (1956), who describe the case of a man presenting with diabetes and hyperlipæmia, who developed hyperglycæmic coma (blood sugar level 681 mg. per 100 ml.) and subsequently died, autopsy revealing pancreatitis. Drouet *et alii* (1956) give an account of an obese man, aged 48 years, who presented with a history of dyspnœa and a recent attack of abdominal pain. He was found to have albumin and traces of sugar and acetone in his urine, with a blood sugar level of 454 mg. per 100 ml. The treatment was as for diabetic coma with relatively large doses of insulin; but his condition deteriorated, and he died after 22 hours. The autopsy showed unexpected hæmorrhagic pancreatitis. A further somewhat similar case history has been reported recently (Sash, 1959); he describes the case of an elderly woman treated with corticoids for rheumatoid arthritis, who developed glycosuria. After some weeks the patient was admitted to hospital, comatose, with a blood sugar content of 1290 mg. per 100 ml. and marked glycosuria, but only slight ketonuria. The treatment was as for diabetic coma, and hydrocortisone was given in addition. Despite this, the patient died after 36 hours, and autopsy showed hæmorrhagic pancreatitis with fat necrosis. Diabetic acidosis itself may be complicated by pancreatitis. This suggests a bad prognosis, and may be the cause of the abdominal pain experienced in some cases of diabetic precoma (Warren, Fallis and Barron, 1950).

It would be expected that permanent diabetes could result from a single attack of pancreatitis, and this has been estimated by Littman (1959) as occurring in 2% of cases. In Pollock's (1959) analysis, six patients went on to develop permanent diabetes after pancreatitis, and at least two required insulin. Another patient developed diabetes after three years, and a known diabetic subsequently required a bigger dose of insulin. In the three surviving patients described by Warren, Fallis and Barron (1950), two required permanent insulin therapy, although one of these had several attacks and did not develop diabetes immediately. This later development of diabetes with recurrent acute pancreatitis is an established entity (Dreiling and Janowitz, 1956; Ivy and Gibbs, 1952; Mackenzie and Wilcox, 1956), and also occurs in chronic pancreatitis (Wirt, Smith and Cooper, 1955).

Clinical Record.

The patient, a married woman, aged 60 years, was admitted to hospital in the evening of May 1, 1959, in a drowsy condition, complaining vaguely of right-sided chest pain and vomiting. The history, difficult to obtain, had begun three weeks before with vomiting, dysuria, cough and a rise in temperature. "Flu" was diagnosed, and a parenteral course of penicillin was given. There was initial improvement; but two weeks later severe dysuria required pethidine for relief. The patient, examined again by her general practitioner, was treated with sulphonamides for cystitis; but soon afterwards the vomiting recurred, and she became confused and disorientated on the day before her admission to hospital. There was no history of abdominal pain, gall-bladder disease or alcoholism. The past history included a radium menopause in 1946, thyroidectomy in 1949, urinary infection and cystoscopy in 1953, and an admission to hospital two months previously with cystitis, cervicitis and senile vaginitis. There was no glycosuria at that time.

On examination, the patient was seen to be a drowsy, dehydrated, obese woman with a cold, clammy skin and a temperature of 96° F. She was grunting as though in pain, and was confused, but realized her whereabouts. Abdominal examination revealed slight generalized tenderness, more marked initially in the left hypochondrium, faint and infrequent bowel sounds, a white vaginal discharge and vulvo-vaginitis. There were no palpable masses, and the femoral pulses were present and equal. The pulse rate was 90 per minute (auricular fibrillation—regular rhythm two months before), and the blood pressure 110/70 mm. of mercury (190/100 mm. two months before). The respirations numbered 30 per minute, and there were a few crepitations at both lung bases. The urine contained sugar (1%) and a trace of albumin; it reacted to Rothera's test, but not to Gerhardt's test. The blood sugar content, rechecked twice, was 1500 mg. per 100 ml. Examination of other systems, including X-ray examinations of the chest and abdomen, gave normal findings.

The clinical problem was therefore that of a shocked, dehydrated, semi-comatose woman, with a very high blood sugar level, but no gross ketonuria, and a strong suggestion of an abdominal catastrophe. The provisional diagnosis was acute pancreatitis or an abdominal vascular occlusion complicated by a diabetic state, or the reverse, and a decision against laparotomy was made. Accordingly the treatment was directed at the relief of pain and shock and correction of the metabolic abnormality.

The patient was treated with pethidine for pain, gastric aspiration, physiological intravenous infusions of sodium, potassium and calcium chlorides, prophylactic administration of penicillin, and initially large doses of insulin given on some occasions by the intravenous route. By the next morning the blood sugar level had fallen to 1040 mg. per 100 ml., the urine was almost free of sugar and ketones, and the serum potassium level was normal. Twenty-four hours after her admission to hospital the clinical condition had not improved, although the blood sugar level had fallen to 380 mg. per 100 ml., and there was no ketonuria. The pulse began to rise, but reverted to normal rhythm, and the blood pressure fell to 80/60 mm. of mercury, the patient remaining semi-comatose with a poor urinary output, no change in the abdominal signs and a normal temperature. The treatment at this time was as follows: the administration of Ringer's solution in 5% dextrose solution, oxytetracycline and hydrocortisone sodium succinate by intravenous infusion, and regular insulin (20 units every eight hours). However, deterioration continued, and methedrine, then noradrenaline, were added with no effect. The patient died 42 hours after her admission to hospital.

Autopsy.

At autopsy, the pancreas was grossly hæmorrhagic with areas of fat necrosis around it. Most destruction occurred in the tail of the organ, where it merged with the left adrenal gland in a diffuse hæmorrhagic mass. Widespread hæmorrhagic areas were seen in the peritoneum covering the stomach, the anterior abdominal wall and the pelvis. The gall-bladder contained numerous large cholesterol stones, and there was some dilatation of the whole of the alimentary tract. Apart from generalized œdema of the lungs there were no other significant findings. Histological examination confirmed the diagnosis of acute hæmorrhagic pancreatitis.

Comment.

It is interesting to note the presence of gall-stones at autopsy. The association of pancreatitis and cholelithiasis has been estimated as high as 80% (Arkin, 1953) and has been described by other authors.

The discrepancy between the height of the blood sugar level (1500 mg. per 100 ml., subsequently 1040 mg.) and the urine sugar content (1%, subsequently a trace) is considerable. A similar difference was found by Drouet et alii (1956), but less marked. A further discrepancy existed between the semi-comatose condition, the high blood sugar level and the only moderate ketosis. In the case described by Sash (1959) the picture was similar.

Perhaps corticosteroids should be used with caution in this condition, as it has been suggested that they themselves may cause pancreatitis (Pollock, 1959; Sash, 1959). If this was so, it is conceivable that pancreatitis could be worsened by their use.

It is debatable whether the high doses of insulin used initially in this case were justified, as the diabetic state in pancreatitis is very labile and hypoglycæmia can easily occur. This in itself could be dangerous, and in addition could stimulate further pancreatic enzyme secretion (Dreiling and Janowitz, 1956). Most authorities agree that insulin should be given with caution and, generally speaking, in small doses (Ivy and Gibbs, 1952; Dreiling and Janowitz, 1956; Berk, 1953).

Pethidine was used as an analgesic instead of morphine to reduce or prevent spasm of the sphincter of Oddi (Ivy and Gibbs, 1952; Dreiling and Janowitz, 1956; Strauss, 1955; Wirt, Smith and Cooper, 1955; Siler, Wulsin and Carter, 1955), but "Banthine" might have been more helpful (Berk, 1953; Dreiling and Janowitz, 1956; Wirt, Smith and Cooper, 1955; Strauss, 1955). Nitrites might have been tried (Mackenzie and Wilcox, 1956; Ivy and Gibbs, 1952).

The patient was adequately hydrated and given replacements of sodium, chlorides, potassium and calcium, but might have benefited by blood transfusion (Wirt, Smith and Cooper, 1955; Dreiling and Janowitz, 1956; Berk, 1953; Strauss, 1955; Arkin, 1953).

Finally, an antitryptic agent might have been of help, such as human serum albumin (Kenwell and Weis, 1953) or soybean trypsin inhibitor (Dreiling and Janowitz, 1956).

Summary.

Glycosuria, hyperglycæmia and impaired glucose tolerance may occur in acute pancreatitis, and permanent diabetes may result. Diabetes may also be associated with other varieties of pancreatitis.

This is the case record of a patient who died 42 hours after admission to hospital with acute hæmorrhagic pancreatitis confirmed by autopsy. The blood sugar level on her admission was 1500 mg. per 100 ml.

Some comments are made on this particular case and on the treatment given.

Acknowledgements.

I should like to thank Dr. Neil Gollan, under whose care this patient was admitted to hospital, for permission to publish the case record, and for helpful advice and criticism, and also Dr. L. Manoim for performing the biochemical investigations.

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Reviews.

The Clinical Syndrome of Diabetes Mellitus. By John Lister, M.A., M.D., M.R.C.P. (Lond.); 1959. London: H. K. Lewis and Company Limited. 8½" × 5½", pp. 244, with 34 illustrations. Price: £1 15s. (English).

THIS is a new publication, which aims to provide a small textbook covering particularly the clinical aspects of diabetes mellitus in a manner which is especially suitable for the student and the family doctor. As such, this book is intermediate in its aims between "Joslin" and Joslin's "Diabetic Manual". There will be students and doctors who find that the "Diabetic Manual" is too colloquial and elementary, while "Joslin" is too detailed and unsuitable for consecutive reading. Some of these will find here a readable, yet reasonably comprehensive, account of diabetes with its complications and management.

The book, which is clearly written, is arranged in three sections comprising diagnosis and treatment, complications and medico-social aspects. The third section is quite brief in comparison with the other two, yet the author does a service in presenting the material in this way and so focusing attention on the socio-economic aspects of diabetic management. It would be a poor diabetic clinic which lacked the services of a trained social worker and a poor clinician who was unaware of the importance of such management.

Though the early chapters are concerned with the history, the ætiology and the biochemistry of diabetes, the approach throughout is essentially clinical, and it is not surprising that the best parts of the book are those concerned with management and complications, and particularly with the more practical aspects of these topics. The student will look in vain for help on some subjects, the specialist will look elsewhere; yet "The Clinical Syndrome of Diabetes Mellitus" has a definite place in the reading of those to whom it is directed. The selected bibliography is well chosen.

The Roots of Crime. By E. Glover, M.D., LL.D. Selected Papers on Psycho-Analysis, Volume 2, 1960. London: Imago Publishing Company Limited. 8½" × 5½", pp. 436. Price: 45s. (English).

THIS lucidly written collection of essays by a leading psycho-analyst, who is an authority on the clinical aspects of criminology, fulfils a long-felt want of a wide variety of workers in the field of delinquency and related problems—social workers, probation officers, doctors, psychologists, psychiatrists, penal reformers, police officers, prison officials and, last but not least, magistrates and judges.

Glover gives an outline of the history of the investigation and treatment of delinquency in Great Britain from the early part of the century to the present day. He includes an important discussion of the report of the Royal Commission on certain aspects of capital punishment, and of the Wolfenden Report. He holds that the Government's response to both of these reports leaves much to be desired, and he elaborates on this. His notes on the M'Naghten Rules are succinctly critical, and he makes constructive suggestions for improvements in these principles based on modern concepts in psychiatry.

Glover describes the expert team-work that is usually necessary to bring about favourable changes in the delinquent, and points out that thorough training, particularly in the workings of the unconscious part of the mind, is important to achieve adequate understanding of the problems. He seems to favour an eclectic approach in psychotherapy, and in selected cases it seems that ten or twenty sessions are often sufficient to bring about a lasting cure, though some patients admittedly need much longer treatment. He deals at length with the psychology of homosexuality, psychopathy and prostitution, and discusses the difficult and important problems of exact diagnosis and consequent prognosis.

Glover rightly points out that scientific criminology is still in its infancy, but that we now know enough to go a long way along the road to prevention if patients are sent for treatment early enough. To this end, he suggests a public health scheme which if implemented, would mean that most potential future behaviour problems would be detected early in school life and adequately treated.

Oral Cancer and Tumors of the Jaws. By George S. Sharp, M.D., F.A.C.S., F.A.C.R. (Ther.), Weldon K. Bullock, M.D., M.Sc. (Path.), and John W. Hazlet, D.D.S.; 1956. New York, Toronto, London: McGraw-Hill Book Company, Incorporated. 9" × 6", pp. 572, with illustrations. Price: $15.00.

THIS book is a very useful addition to the library of the general practitioner and of medical and dental students.

The authors have presented this book in five parts. In the first part they deal with general principles of neoplasia embracing the history of cancer, origin of cancer and classifications of oral neoplasms. There is one section discussing the importance of biopsy and the methods involved. The second part deals with the particular problems associated with neoplasms of the oral mucosa and accessory cavities. The last three parts deal with the pathology of tumours and cysts of the jaw.

Each section deals systematically with the particular anatomical features, possible ætiological factors, pathology, clinical appearances and X-ray appearances. The differential diagnosis, treatment and prognosis are discussed. Considerable trouble has been taken to present excellent plates illustrating the clinical and X-ray appearances.

Treatment is clearly and briefly stated in each section. In the section on antral carcinoma there should be some mention of the place of less radical procedures, such as antrostomy and irradiation. However, the authors have written this book as a guide to the diagnosis of oral cancer and benign tumours rather than as a discussion of the various methods of treatment.

The Hæmolytic Anæmias: Congenital and Acquired. Part I. "The Congenital Anæmias." By J. V. Dacie, M.D. (Lond.), F.R.C.P. (Lond.); Second Edition; 1960. London: J. and A. Churchill Limited. 8¾" × 5½", pp. 348, with 118 illustrations. Price: 45s. (English).

MANY of us in Australia have come to look on Professor J. V. Dacie's Department at the Postgraduate Medical School, London, as a source of inspiration necessary to all hæmatologists, and we have awaited eagerly the second edition of this book. This edition, which succeeds the first edition of 1954, has been expanded into two volumes. The fact that Part I, which is reviewed here, deals solely with the congenital hæmolytic anæmias reflects the great advance in knowledge of these diseases that has taken place in the last decade.

This volume brings us up to date on the laboratory investigation and clinical features of these disorders. Thus it gives a valuable review of the application of isotope techniques to the understanding of "erythrokinetics". As an example, the destruction in the spleen of red cells labelled with radioactive chromium is measured by surface counting over the spleen. By this method the desirability of splenectomy may be assessed. The basic metabolic changes in erythrocyte metabolism associated with these anæmias are described.

The rarity and complexity of the congenital non-spherocytic group has not deterred investigators, including Professor Dacie and, in Australia, Dr. G. C. de Gruchy, from making inroads into our understanding of them. The clinical syndrome of thalassæmia minor, which now confronts us in this country with our progressive immigration policy, is lucidly described. However, we still await the development of more definitive methods of diagnosis.

Professor Dacie has clearly set out the diseases caused by the presence of abnormal hæmoglobin—the "hæmoglobinopathies"—explaining the many new terms which confront, indeed often confuse, the clinician of today.

Throughout this volume there are sound clinical descriptions and some splendid case histories, which should prove of value to the practising physician in the management of his patients.

This is an excellent book, which can be highly commended to all pathologists, physicians and biologists. The bibliography is a monument to Professor Dacie's erudition, and reflects the contribution he and his colleagues have made in this field. Both author and publishers are to be warmly congratulated on the excellent reproduction of the 118 illustrations. We look forward to receiving Part II.

Oxygen Supply to the Human Fœtus: A Symposium Organized Jointly by the Council for International Organizations of Medical Sciences Established under the Joint Auspices of UNESCO and WHO and the Josiah Macy, Jr. Foundation. Edited by J. Walker and A. C. Turnbull; 1959. Oxford: Blackwell Scientific Publications Limited. 8¾" × 5½", pp. 326, with illustrations. Price: 47s. 6d. (English).

THIS book, although not uniform in series with other Josiah Macy symposia, is marked by the same frank and critical discussion at the conclusion of each paper that distinguishes these symposia and the CIBA colloquia.

The main interest in this book will be for the respiratory physiologist working in obstetrics, rather than for the clinical obstetrician. There is a valuable section on the limitations of present methods of measurement of uterine blood flow and the methodology of cord oxygen determinations. It is clearly indicated that much of the conflict initiated by the original observations of Walker and Turnbull still awaits resolution. One of the main difficulties lies in knowing how far back in intrauterine life cord studies at the time of birth can be extrapolated, and here, clearly, lies the disadvantage of this method of approach.

The work of Hon and his associates on continuous fœtal heart rate patterns in labour, which has appeared since this conference in 1957, indicates that hope of progress in this important facet of fœtal physiology lies in studies during labour. It is hoped that efforts to correlate studies of intervillous blood and fœtal heart rate patterns during labour will prove of more value in the future than studies of cord-blood oxygenation at the time of birth have proved in the past.

Diagnosis in Locomotor Disorders. By Kenneth Stone, D.M. (Oxon.), M.R.C.P.; 1960. London and Melbourne: Oxford University Press. 8½" × 5½", pp. 230, with 53 illustrations. Price: 41s. 6d. (Aust.).

PHYSICIANS specializing in the field of rheumatic diseases are impressed by the wide range of conditions other than the main groups of arthritic diseases which they see in hospital clinics and private practice, the differential diagnosis of which covers many different fields of medicine. The purpose of this book is to discuss the diagnosis of the diseases which present with symptoms and signs involving the locomotor system. No attempt has been made to include prognosis and treatment. This would have resulted in considerable enlargement of the text, and would have defeated the main purpose in providing a quick and well-arranged reference for practitioners confronted with these problems.

The material is arranged alphabetically by symptoms, starting with "Aching, Generalised" and ending with "Spasticity". To avoid repetition certain conditions are described under one heading, and cross references are given in the text where applicable for the same disease, which may present with other symptoms. A good index facilitates the location of any condition not readily found in the text. Tables, line drawings and reproductions of X-ray plates are used where necessary, although the last-mentioned are not very satisfactory.

The individual descriptions of the diseases causing the various symptoms and signs are masterpieces of lucid and succinct writing, reflecting great credit on the British school of medicine which rightly emphasizes the clinical aspects of history-taking. One admires the emphasis placed on points of considerable diagnostic importance which have come from the author's own experience rather than from the descriptions usually found in standard textbooks.

While arranged as a reference book, this work is eminently readable and should do much to make general practitioners aware of the many diseases which may at first sight appear to fall within the group of arthritic disease. Many of these conditions are responsive to treatment, and their recognition may well result in great benefit to the patient. Dr. Stone is to be commended on an original and valuable contribution to the literature on the subject.

Diseases of the Skin. Edited by Marion B. Sulzberger, M.D., F.A.C.P. (*The Medical Clinics of North America*, May, 1959, Vol. 43, Number 3). Philadelphia and London: W. B. Saunders Company. Sydney: W. Ramsay (Surgical) Limited. 8¾" × 5½", pp. 633-698, with 161 illustrations. Price (6 issues per annum): Paper binding £6 15s., cloth binding £8 2s. 6d.

THIS number of *The Medical Clinics of North America* is devoted to a symposium on diseases of the skin, with M. B. Sulzberger as Guest Editor. In the foreword it is stated that the principal objectives in selecting topics for the issue were (i) to indicate the wide range of the problems, techniques and skills encompassed by modern dermatology, (ii) to highlight both the relationships and the differences between dermatological problems and those of other fields of medicine and surgery and (iii) to provide a glimpse of the great advances which have been made in the fundamental understanding and in the prevention and treatment of skin diseases, and to indicate the influence of these advances on other fields of medicine. Of the 21 contributions, the first five are concerned with general topics, such as "Some Physiological and Clinical Aspects of the Water and Electrolyte Contents of the Skin" and "Principles and Practice of Topical Dermatological Therapy"; the remainder deal with more specific problems, ranging from "Disturbances of Melanin Pigmentation and Their Management" and "Genodermatoses" to "The Management of Acne Today" and "The Problem of Psoriasis". This book offers authoritative information on a wide selection of dermatological topics for anyone wishing to bring himself up to date in this field or to refresh his knowledge on any of the particular subjects discussed. There is a useful selection of black-and-white photographic illustrations.

Handbook of Neurological Diagnostic Methods. Edited by Fletcher McDowell, M.D., and Harold G. Wolff, M.D.; 1960. Baltimore: The Williams & Wilkins Company. 9" × 5¾", pp. 210. Price: 49s. 6d.

THE preface of this manual states that about 15% of those who die each year in the United States of America die as a result of defects in the nervous system, and emphasizes that pride in craft should lead the physician to approach the nervous system with knowledge and eagerness rather than the "frightened ignorance" of the past.

The book first outlines the method of history-taking and examination used in Cornell Medical College. Physical examination proceeds from head to foot, dealing with receptor and effector functions at each level. This seems more cumbersome, and the results seem harder to evaluate, than the traditional British system, but the authors give reasons why it is preferred. Special investigations are then discussed in random order, with very few connecting links to help the student plan them in relation to a clinical problem. There is a comprehensive table of cerebro-spinal fluid abnormalities in the chapter on lumbar puncture. The section on skull radiology is brief to the point of omitting reference to special views—for example, of the petrous temporal bone—and would be enhanced by a table of causes of intracranial calcification. Contrast radiography also receives little space compared with the excellent chapter on visual fields which follows. Other subjects discussed are electroencephalography, electromyography, audiometry (without mention of loudness balance tests), caloric labyrinthine responses and cystometry. Quantitative testing of the sense of smell, the demonstration of sweat levels and the examination of the aphasic patient are considered.

The book then branches out into the management of some neurological emergencies, and ends with a quiz, which is provocatively entitled "Irreducible Minimum of Information Esssential to an Intelligent Understanding of Diseases of the Nervous System". It would be an exceptional student who could attain this irreducible minimum and answer such questions as: "Discuss the metamorphosis of the microglia in health and disease."

In summary, this book is a guide to the practice of neurology at Cornell and is, therefore, of great interest

to those who teach this subject. It contains much valuable information which is not often found in standard textbooks; but the approach is sufficiently different from ours to limit its value for Australian students.

Body Fluids in Surgery. By A. W. Wilkinson, Ch.M., F.R.C.S.E., F.R.C.S.; Second Edition; 1960. Edinburgh and London: E. and S. Livingstone, Limited. 8¾" × 5¼", pp. 288, with 12 illustrations and 30 tables. Price: 21s. 6d. (English).

Every surgeon is continually perplexed in his practice by problems of salt and water balance, and neither by training nor by inclination is he usually equipped, in terms of biochemistry, to make much sense out of them. Like the alchemist of old, he relied for a time on the touchstone of the urinary chlorides, only to learn that this was not only useless but misleading. Later, with the advent of the flame photometer in pathology laboratories, he became familiar with serum levels of sodium and potassium, only to be told that these gave very little guide to the quantitative losses in the body. Now he is faced with ignoring the fundamentals entirely and soothing his conscience with rules of thumb, or learning the basis of this new physico-chemical understanding which has grown up in the last few years. Professor Wilkinson's book is expressedly a primer for this purpose. It sets out, succinctly and pictorially, firmly established knowledge, together with the gaps, which enable the clinician to assess the biochemical deficits. He reviews the handling of water, sodium, potassium, chloride and acid base balance; it is stressed that this is a dynamic equilibrium, and that quantities are as important as concentrations; in fact, this first part of the book is essentially one of chemical physiology. The known facts are then integrated with the clinical problems of shock, gastro-intestinal losses, and response to operation in both the adult and in the child. Principles and details of management of water and salt replacement are set out with some clarity.

This book represents a reasonable compromise between the specialized monograph and the encyclopædic tome. Though its style makes for hard and concentrated reading in parts, it can be safely recommended as a balanced introduction to this continually expanding field.

First Aid: Diagnosis and Management. By Warren H. Cole and Charles B. Puestow; Fifth Edition; 1960. New York: Appleton-Century-Crofts Inc. 8¼" × 5¼", pp. 432, with illustrations. Price not stated.

First appearing in 1942, this manual, in the latest edition, has been thoroughly revised and largely rewritten. Many new illustrations have been added. The book is one for the experienced first-aider, the well-trained ambulance room attendant, the member of the Army Medical Corps, the nurse and even the newly-qualified medical practitioner, rather than for the new trainee in first-aid. It would be very useful in the instruction of members of civil defence organizations.

The anatomy and physiology of the human body and the principles of the first-aid treatment of wounds, hæmorrhage and fractures are competently described. The immediate covering of wounds and the use of dry sterile dressings to cover them before the patient's dispatch to hospital are advised, and the use of the pad and bandage in the control of hæmorrhage is emphasized. The prevention of shock and its treatment is dealt with in accordance with modern ideas. The importance of blood transfusion as an urgent measure in severe injuries is stressed.

A description of the types of Army, Navy and Air Force missiles and rockets as at present developed in the United States, as well as of nuclear bombs and their effects, forms a modern and interesting chapter. The effects of exposure to various intensities of radiation from the latter are described. Chemical warfare is not forgotten, and the description of the types of gases and the treatment of chemical warfare casualties is adapted from an Army Technical Manual. Mass casualty problems are described. In fact, the first-aid aspects of national civil defence form a most valuable portion of the manual. A bibliography to this chapter gives references to the publications of the United States Government Departments concerned with civil defence up to as recently as 1958.

The chapter discussing respiratory emergencies, for which Archer S. Gordon is responsible, is outstanding, as would be expected. Expired air inflation of the lungs in the treatment of asphyxia, a newcomer to first-aid manuals, is fully discussed. The importance of the fully extended head in both expired air and manual methods of resuscitation is stressed both in the text and by illustration.

Subjects not usually discussed in first-aid manuals are medical emergencies, the examination and treatment of the "prostrate" patient and the first-aid treatment of industrial injuries.

The book concludes with a chapter "Civilian versus Military Casualties", in which some thought-provoking statistics are given. It is pointed out that accidents in the United States rank fourth in the causes of all deaths, being exceeded only by heart disease, cancer and cerebral hæmorrhage. From Pearl Harbour to V.J. day, there were 79,622 more civilian deaths from accidents in the United States than total military deaths for the same period. In 1958, there were 91,000 accidental deaths, 37,000 of these being the result of automobile accidents.

This is an excellent publication, and its use is strongly recommended. The illustrations (line drawings) are instructive and the index is adequate.

Cancer Current Literature Index. Under the general editorship of W. van Westering; 1959. Amsterdam, New York: Excerpta Medica Foundation. 9¼" × 6¼", pp. 38. Price: $7.50 per year (subscription).

This Index is sponsored jointly by the American Cancer Society and the Excerpta Medica Foundation, and is an attempt to make known with the absolute minimum of delay the titles of reports in the world's medical literature throughout the whole field of cancer. It takes the place of *Current Cancer Literature*, which ceased publication in 1955. It is intended to bridge the gap between the publication of original articles and their appearance in abstract form in Excerpta Medica's cancer-abstracting section. This Index began publication in September, 1959, and it is intended that fresh numbers should appear every two or three weeks. Articles from some 3000 medical journals, including those from the U.S.S.R., will be listed, and it is anticipated that at least 4500 references will be provided each year. This number may shortly increase, as the Excerpta Medica Foundation is making arrangements to provide expanded, and ultimately complete, coverage of the cancer literature of Japan and China. To assist readers, all titles are listed according to a prescribed system, Chapters I to X contain reports on general subjects, and Chapters XI to XXX are devoted to the various organ systems. Each reference gives the title (with a translation if the title is not in English), full references, and the name(s) of the author(s). Though for most purposes abstracting journals will be the more informative, this Index should prove a valuable aid in the never-ending task of keeping track of new publications.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"The Early History of Surgery", by W. J. Bishop; 1960. London: Robert Hale Limited. 8½" × 5¼", pp. 192 with illustrations. Price: 18s. net (English).

"Progress in Psychotherapy", edited by Jules H. Masserman, M.D., and J. L. Moreno, M.D.; Volume V. Review and Integrations, 1960. London and New York: Grune & Stratton. 9" × 6", pp. 262. Price: $8.50.

"The Divided Self: A Study of Sanity and Madness", by R. D. Laing; 1960. London: Tavistock Publications; Melbourne: The Melbourne University Press. 8½" × 5½", pp. 240. Price: 25s. net (English).

"The Purpose and Practice of Medicine", by Sir James Spence, with a memoir by Sir John Charles; 1960. London, New York, Toronto: Oxford University Press. 8½" × 5½", pp. 320, with illustrations. Price: 68s. (English).

"Miscellaneous Notes (Seventh Series)", by F. Parkes Weber, M.D., F.R.C.P., F.S.A.; 1960. London: H. K. Lewis & Co. Ltd. 7¼" × 4¾", pp 12. Price: 3s. net (English).

"Dental Practitioners' Formulary 1960: For Use in the National Health Service"; 1960. London: The British Medical Association and The Pharmaceutical Press. 6½" × 4", pp. 56. Price: 3s. 6d. (English).

"Automatic Chemical Analysis", edited by Ralph H. Muller; *Annals of the New York Academy of Sciences*, Volume 87, Art. 2, July 22, 1960. New York: New York Academy of Sciences. 9" × 6", pp. 609-951, with illustrations. Price: $3.50.

The Medical Journal of Australia

SATURDAY, OCTOBER 8, 1960.

CARE OF THE AGED AND CHRONICALLY ILL.

THE problem of the care and rehabilitation of the aged and chronically ill is approached with commendable realism and humanity in a report prepared by the New South Wales Director-General of Public Health, Dr. C. J. Cummins, and recently made available. It is, indeed, encouraging to see such a report from a government department, and the New South Wales State Government will do a great service to the community at large, in addition to the group of citizens primarily concerned, if it is able to implement the Director-General's ideas fully and in the spirit in which they are put forward.

The realism of the report appears immediately in its initial statement of the problem. The care of the aged and chronically ill has been a problem in every age in socially responsible communities, but the contemporary scene presents its particular and even unique features. The relative increase in the aged group (65 years and over), especially in proportion to the working age group, is generally known, but its extent and its social significance are probably not as fully appreciated as is warranted. It is a major factor in the pattern of modern society. Paradoxically, the social problems which it creates are aggravated, not alleviated, by the prosperity of our community. "The economic climate created by a widespread release of prosperity", the report asserts, "brings in its train certain social reactions which have an adverse influence on the welfare and security of the elderly and less productive members of the community". These reactions the report sets out with care, and we need not follow them in detail. The essence of them is that everyone is engaged in a mad rush to take the fullest advantage of material prosperity and of the high standard of living that is taken for granted. The less fortunate members of the community, "who cannot share, or contribute towards gaining their proportionate share of the prosperity offering because of age or physical and mental incapacity . . . represent a burden upon the family socially and economically,—a burden which is often considered intolerable when their incapacity interrupts or hinders family security or comfort". Put bluntly this means that prosperity breeds selfishness, though there are qualifying aspects of the matter, and the community creates for itself a problem which it must in turn solve—or rather which its more responsible members have to solve. The practical situation is summed up thus in the report: "The conscience of the community willingly accepts the principle that elderly and incapacitated citizens face their burdens alone, or that they should be cared for outside the family environment by charitable and denominational organizations, by the State, or by private hospitals and convalescent homes."

The report goes on to analyse the available accommodation for the care of the aged and chronically ill as provided by the Government, by religious bodies and by various voluntary charities, and shows that the greatest, though not by any means the only, problem relates to the demand for beds for those, whether aged or otherwise, who are suffering from long-term illness. There appears to be saturation of available accommodation of this kind with long waiting lists and long prospective periods of waiting. The report comments that the resolution of this problem is difficult, and will not be approached unless there is a coordination of effort of the various agencies in the field and a reorientation of thought towards sharing and diverting the burden. With this, it continues, must be associated a sustained effort to condition the community conscience to retain or receive again a greater proportion of those concerned in the domestic environment. To achieve this purpose coordination of activities of all agencies working in this field is required, together with a community educational campaign and a rehabilitation programme for the aged and chronically ill to prepare them for reception into the domestic environment, or to condition them to withstand the socio-economic stresses of that environment.

After the introductory section the report goes on to an examination of the various agencies working in this field, and the contributions they are able to make to it, showing a sympathetic understanding of their several points of view. It then considers the question of rehabilitation as it affects the class of people under consideration in this report. It lays stress on preventive aspects of rehabilitation, including the need to condition well aged persons to adapt themselves to the various destructive influences—degenerative processes and psychic stresses—to which they are exposed. It points out that rehabilitation can have some effect even on the more hopeless group; for example, the regaining of voluntary control of bladder and bowel function can relieve the burden of nursing and restore dignity and hope to a patient. Reference is then made to a programme of rehabilitation being planned by the Department of Public Health in New South Wales. This is to be centred round Lidcombe State Hospital, where a Department of Physical Medicine is to be established. Other State hospitals are to be integrated into this plan. The aim of the programme is to assess the rehabilitation potential of every patient admitted to a State hospital, and to classify and dispose of the patient accordingly, "subject of course to certain social criteria such as the wish of the patient, accessibility to kin and visitors, etc.". An assurance is given that safeguards will be adopted to ensure that the patient is regarded as a human being and not as an impersonal medical unit, and that the emphasis on human dignity will be maintained at all times. It is hoped to devise a means of bringing the denominational and voluntary organizations also into effective contact with the Department's rehabilitation programme.

The report then broadly outlines seven principles on which, in the Director-General's opinion, an appropriate State plan should be based. The first is that the care of the long-term chronically ill should be included in the plan as well as the care of the aged. The second is that the basic approach must be preventive; measures are necessary to postpone deterioration or to delay aggravation of disability. The third is that emphasis must be diverted from institutional care to maintenance of the aged in a domestic or simulated domestic environment. The fourth is that care of the chronically ill should not be divorced from general medical care if the highest standards are to be maintained. The fifth is that the cost of programmes for the care of the aged and chronically ill should be measured in terms of human values and not productivity; the objective is the return of the person as quickly as possible to social adaptations. The sixth is that maximum use should be made of the experience and resources of the many agencies already active in this field; their resources could sometimes be more efficiently used, and they should be represented on any State advisory body. The seventh is that the care of the aged and chronically ill should be considered as an attribute of social welfare with special medical emphasis, and therefore as a public health problem although other State social agencies come into it; there would seem also to be a greater role that could be played by the Commonwealth, particularly in relation to financial assistance.

The Director-General suggests that an organization to implement these principles could be designed within the framework of the administration of the Department of Public Health, and that it should be divorced from the administration of the general hospital system. It would comprise two components: a Division of Geriatrics and Gerontology, and an Aged Persons Welfare Committee. The Division of Geriatrics and Gerontology would integrate, coordinate and supervise departmental agencies already operative or proposed. These would include the following: State hospitals; rehabilitation; private hospitals and rest homes as registered under the *Private Hospitals Act*, 1908, as amended; the Consultative Council for the Physically Handicapped; the Hospitals Admission Depot. In addition the Director of the Division of Gerontology and Geriatrics would be chairman of the Aged Persons Welfare Committee, and the Division would perform the executive functions for that committee. The function of the Aged Persons Welfare Committee would be the integration and coordination of all activities in the fields of gerontology, geriatrics and chronic diseases. It would need to have a wide representation, including Government departments already active in the field, as well as representatives of the religious and voluntary agencies, semi-official social welfare organizations, local authorities and the universities. It would also need a considerable amount of finance. It is suggested that its function could include the distribution of finance for geriatric and gerontological research, and for fellowships in these fields, the organization of publicity and health education on the problems of the aged and aging, and the provision of financial assistance towards the establishment of geriatric annexes and institutions and like projects for the aged and persons suffering from long-term incapacitating chronic diseases. For the last-mentioned purpose, financial assistance would be towards the establishment of hospital type units as distinct from homes for the well aged, which already receive finance from the Commonwealth Government under the *Aged Persons Homes Act* of 1954. It is pointed out that a State formula would have to be devised for such assistance similar perhaps to that in operation in Queensland, with or without Commonwealth assistance. Only those agencies which conformed to the requirements of the committee would be eligible for such assistance, and capital assistance would be on a pro-rata basis to voluntary raising.

It is clear that a great deal more detail would have to be worked out before this plan could come into full operation, and no doubt an element of trial and error would operate for a considerable time. Nevertheless, the plan in its broad aspects is constructive and stimulating. It could of course be said that the essence of the plan was the formation of just another government-dominated committee with resultant threats of bureaucratic control and suppression of private initiative. However, the report just has not that atmosphere. It appears to be a genuine and informed attempt to cope with a difficult but pressing situation, in full appreciation of human values. Thoughtfully developed, provided reasonable financial provision was made, the suggested plan could mean the efficient and wise use of government resources and the freeing of voluntary agencies from much of their burden of inadequacy of resources and financial strain, so that they could get on with the job that they have been doing so faithfully and well despite severe handicaps.

Current Comment.

THE "LOW SALT SYNDROME" IN CONGESTIVE CARDIAC FAILURE.

Hyponatræmia in congestive cardiac failure occurs principally in the terminal stages of the natural history of heart disease. In some instances it may occur as a transient event, when it may be reversible with appropriate therapy. The management of this important condition is discussed in a recent review by E. H. Luckey and A. L. Rubin, included in a symposium on congestive heart failure published by the American Heart Association.[1]

The "low salt syndrome" is characterized by œdema resistant to diuretic therapy, increasing body weight, raised blood urea nitrogen level and decreased urea clearance, and a fall in plasma sodium and chloride levels. Because hyponatræmia was usually associated with intensive therapy, early experience suggested that it was due to excessive sodium loss during diuresis, particularly with mercurial diuretics, in patients on low sodium diets. Although each of these factors may play a part in the development of hyponatræmia in some patients, there is now general agreement that the most important cause for this condition is an inordinate retention of water. The plasma sodium concentration is low, but the total amount of extracellular sodium remains higher than normal; hence water is present in even greater excess. This consideration has led to the proposal by L. Leiter *et alii*[2] of the term "dilution syndrome" instead of "low salt syndrome".

Luckey and Rubin point out that since the extracardiac mechanisms responsible for the disturbance in handling water are the result ultimately of the cardiac status of the patient, then any measure which may be useful in improving cardiac efficiency should be helpful in correcting

[1] "Symposium on Congestive Heart Failure", edited by Herrman L. Blumgart, M.D.; American Heart Association Monograph No. 1; 1960. New York: The American Heart Association. 10¼" × 7¼", pp. 128, with illustrations. Price: not stated.

[2] *Bull. N.Y. Acad. Med.*, 1953, 29: 833 (November).

hyponatræmia. Therefore attention should be directed towards a careful study of the nature of the heart disease, including factors contributing to failure and a reevaluation of the therapeutic régime during which the hyponatræmia developed. Transient periods of myocardial deterioration may occur with intercurrent infections, pulmonary infarction and other processes that impose an added burden on the failing heart. Hyponatræmia may occur during such easily recognizable episodes; hence these processes should be sought and treated as vigorously as possible.

In the absence of an obvious cardiac cause of the condition which may be amenable to treatment, the earliest suggested therapy was the liberalization of dietary sodium intake or the slow intravenous administration of hypertonic saline, after which a response may occur in some patients, but generally diuresis does not occur. The sudden increase in extracellular fluid withdraws water from the body cells, causes intense thirst, and commonly results in excessive fluid intake and a progressive increase in body weight with persistent hyponatræmia. Furthermore, the increase in plasma volume with intravenous administration of hypertonic sodium chloride may be sufficient to produce acute pulmonary œdema. In the opinion of Luckey and Rubin, intravenous administration of sodium chloride is never justified and should be condemned. The régime recommended for patients with hyponatræmia and hypochloræmia is the elevation of the plasma chloride level towards normal with non-sodium chloride salts, which will result in acidosis and a progressive increase in urinary chloride concentration. Fluids should then be restricted so as to approximate insensible losses, after which administration of a mercurial diuretic will result in diuresis with the urinary sodium value hypotonic in comparison with the plasma sodium value. Such a diuresis over a period of days is followed by a rise of plasma sodium content and a decrease in body weight. Ammonium chloride is commonly used to produce such acidosis, but there is a significant incidence of gastrointesinal intolerance due to ingestion of the 10 to 12 grammes required. Furthermore, if hepatic insufficiency is present, liver failure may be precipitated. Both calcium and potassium chloride have been used as substitutes for ammonium chloride, and although each will raise the chloride level in the plasma, there are disadvantages. Calcium chloride is even more irritating to the intestine than is ammonium chloride, while potassium chloride may produce dangerous levels of hyperkalæmia if there is renal insufficiency with low urinary volumes.

If none of the above salts can be used, there is now fortunately available a chloride salt with minimal gastrointestinal side effects and none of the disadvantages of the ammonium, calcium or potassium salts. This is the monohydrochloride of *l*-lysine. Although it contains less chloride ion than the salts discussed previously, large doses can be tolerated, and no untoward effects due to the lysine ion have been encountered. Further trials with this new lysine salt are awaited with interest, and should its further use prove it to be as free of side effects as is indicated in this paper, then another significant advance in the therapy of resistant cardiac failure will have been achieved.

DANGERS OF HORMONE ADMINISTRATION DURING PREGNANCY.

A YEAR AGO we commented[1] in these columns on the danger of inducing masculinization of a female fœtus by the exhibition of potentially androgenic hormones during pregnancy. The trap of course is that androgens and progestogens are chemically closely related, and that among the somewhat bewildering array of synthetic hormone preparations available, many of those designed primarily for gynæcological conditions have in fact some androgenic properties as well. The use of progesterone in the treatment of threatened or habitual abortion was one of the early applications of hormone therapy, but it met with indifferent success, partly because daily injections were necessary to maintain a reasonable blood level of the hormone. Since then a variety of synthetic progestogens have been developed which can be given effectively by mouth.

Most of the first-reported cases of masculinization of the female fœtus followed the use of methyltestosterone in cases of habitual abortion. With the introduction of the synthetic progestogens there was no longer any reason to use a hormone with such frankly virilizing properties. However, the synthetic progestogens are closely related to testosterone, and the possibility of a masculinizing effect on a female fœtus when some of these are given in early pregnancy now appears abundantly documented. In 1958 L. Wilkins and his colleagues[2] published a series of 17 cases in which varying degrees of masculinization had followed the use of progestogens in early pregnancy. In 15 of these cases the preparation used was ethisterone (17-α-ethinyl-testosterone). Wilkins has now published a further report[3] in which he has collected data on 70 cases of fœtal masculinization of female infants following the oral administration of progestogens to their mothers during pregnancy. This series includes 31 cases in which masculinization followed the exhibition of ethisterone, and 35 in which it followed the exhibition of norethisterone (17-α-ethinyl-19-nortesterone). The criteria used to exclude adrenal abnormality as the cause were (i) the demonstration of "chromatin-positive" type nuclei in the buccal smear and (ii) the finding of normal levels of 17-ketosteroids in the urine.

In his earlier study, Wilkins included two cases in which masculinization followed the intramuscular injection of progesterone as the only treatment given to the mother. He has also observed four cases of fœtal masculinization in which no hormones were given and there was no evidence of adrenal abnormality. In such cases it may be necessary to postulate abnormal metabolism of either endogenous or exogenous progesterone by the mother to form androgens. However, such cases are rare beside the frequency with which masculinization may follow the use of some synthetic progestogens, and Wilkins expresses the opinion that norethisterone has caused fœtal masculinization with sufficient frequency to preclude its use or advertisement as a safe hormone to be taken during pregnancy. He states that the older compound, ethisterone, has caused masculinization comparatively infrequently, but that its potential hazard should not be forgotten.

The most important aspect of the whole matter is that those concerned should be aware of the possibility of fœtal masculinization due to exogenous hormones, and that the correct diagnosis should be made at the beginning (female infants in such cases can be, and have been, diagnosed as male with hypospadias and undescended testicles). Wilkins states that even in the most severe cases surgical correction is relatively simple, there is no progressive virilization, and such patients will eventually mature into normal females. Wilkins makes the point that without hormone treatment some of these patients might never have been born at all, so that the risk of producing a correctable deformity can be justified in certain cases. However, the existence of the hazard should be recognized. This hazard is largely avoided if it is possible to postpone the use of hormones till after the twelfth week of pregnancy. In the series studied by Wilkins labio-scrotal fusion occurred only when administration of the hormone had been begun before the twelfth week of pregnancy. Phallic enlargement can result when androgenic activity is exerted over a sufficient period at any time during fœtal or post-natal life. However, in cases in which a female infant is born with an enlarged clitoris, the general experience appears to be that this tends to correct itself automatically as growth proceeds, once the influence of the extrinsic hormone is withdrawn.

[1] MED. J. AUST., 1959, 2:20 (July 4).

[2] *J. clin. Endocrin.*, 1958, 18:559 (June).

[3] *J. Amer. med. Ass.*, 1960, 172:1028 (March 5).

Abstracts from Medical Literature.

OBSTETRICS AND GYNÆCOLOGY.

Sterility and ABO Incompatibility.

S. J. Behrman *et alii* (*Amer. J. Obstet. Gynec.*, May, 1960) have studied 200 infertile couples who had been trying to conceive for at least five years, and in whom no reason for their infertility problem could be determined by exhaustive gynæcological and urological investigation. The authors investigated the possibility of serologically incompatible mating in the ABO system. The presence of naturally occurring antibodies of the ABO system has been detected in almost all the body secretions, including the cervical secretion. These antibodies are most significant in the Type O wife because she may have both the anti-A and anti-B present. Sperms can carry the antigen and these sperms can be agglutinated by ordinary anti-A or anti-B serum. The authors postulate that infertility resulted from incompatibility of an ABO blood group mating at the cervical level, involving most frequently a Type O wife and a Type A or Type AB husband. Of 102 such infertile couples carefully evaluated, 87% were found to have incompatible matings as compared to 38% of 171 fertile couples. In seven additional subfertile couples with incompatible matings who eventually conceived after 10 years of infertility, all the offspring were of Type O. This indicated that the Type A or Type B fathers were heterozygous and the children were born of homospecific pregnancies.

Urinary Deviation in Gynæcological Surgery.

R. Shackman (*J. Obstet. Gynæc. Brit. Emp.*, August, 1959) discusses urinary deviation in gynæcological surgery under the broad classification of fortuitous and planned deviation. Fortuitous deviation may be recognized at operation or may reveal itself subsequently by the development of a fistula—vesico-vaginal, ureterovaginal, utero-vesical or vesico-colic. Planned deviation may be brought about by the operations of ureterostomy, pyelostomy, nephrostomy, uretero-colic transplantation and uretero-ileostomy ("ileal bladder"). Bladder injuries noted during gynæcological operations are sutured at once and an indwelling Foley catheter is inserted for seven days. When the ureter is divided in the region of the uterine vessels the author recommends reimplantation of the ureter into the bladder by a mucosa-to-mucosa single-layer silk stitch using the Coffey tunnel technique through the bladder wall. When the ureter is divided at a more proximal level, or when a length of ureter has been inadvertently resected, reimplantation into the bladder is not possible and the three alternatives are: (i) the use of a closed loop of ileum, anastomosed to the end of the severed ureter proximally and implanted into the bladder distally; (ii) direct ureteral anastomosis if adequate mobilization is possible; (iii) cutaneous ureterostomy as a last resort. The author briefly discusses the not uncommon complications of vesico-vaginal fistula and uretero-vaginal fistula, as well as the rare utero-vesical and vesico-colic fistulæ. Planned deviation of urine in gynæcological surgery is usually performed as part of the surgical treatment of extensive malignant disease of the pelvic organs. Other indications include the relief of ureteric obstruction. Case reports quoted include those of patients treated by temporary nephrostomy for obstructed ureters, one of permanent nephrostomy in a patient with only one kidney, one of transplantation of the ureters into the colon, and one of transplantation of the ureters into an isolated segment of ileum. The author emphasizes certain principles of technique in the operation of uretero-colic transplantation. In cases of complete exenteration, uretero-colic transplantation is considered to afford more comfort to the patient than uretero-ileostomy.

Routine Cytology Smears in Pregnancy.

H. E. Schmitz *et alii* (*Amer. J. Obstet. Gynec.*, May, 1960) report their findings in routine vaginal smears taken routinely from 10,369 ante-natal patients. In all, 105 patients (1%) gave positive or suspicious smears. Patients with positive or questionable smears were investigated further by biopsy until the presence or absence of disease was established. Invasive carcinoma was found in 12 cases and carcinoma-in-situ in 13; this total of 25 cases of malignant change in the cervix during pregnancy represents about one in every 400 obstetric patients. The majority of these lesions were early and curable. Nineteen patients showed basal-cell hyperplasia with positive smears; these were all followed up, and in three cases a cone biopsy of the cervix, taken three months after delivery, revealed carcinoma-in-situ. In two cases there was definite progression from basal-cell hyperplasia to early invasive carcinoma, one in a period of one year and one over a period of three years. Cases in this group should be followed indefinitely. The authors conclude that there seems to be enough carcinoma of the cervix in younger women, especially those bearing children, to warrant the routine examination of vaginal smears in pregnancy.

Bioflavinoid Compounds in Rh-Immunized Women.

W. M. Jacobs (*Surg. Gynec. Obstet.*, January, 1960) reports his further experience with the administration of bioflavinoid compounds to Rh-immunized women. The author refers to a preliminary report on the subject published in 1956. He states that much has been written on the effect of bioflavinoid compounds in the prevention of capillary fragility, and that the mechanism of Rh immunization depends on the entry of fœtal Rh-positive cells into the maternal circulation through breaks in the placental capillary system. Such breaks may occur in normal pregnancy, and the use of bioflavinoid compounds is an attempt to eliminate or reduce the transfer of Rh-positive cells into the circulation of Rh-negative mothers. The author has conducted a trial in which 32 Rh-negative pregnant patients with evidence of previous Rh immunization were given bioflavinoid compounds in doses of 400 to 600 mg. daily. The outcome of their pregnancies was compared with that of 71 pregnant women with similar evidence of previous Rh immunization who were not given bioflavinoid capsules. The patients were divided into three groups according to the severity of the effect of Rh immunization in previous pregnancies, and in each group it was found that those receiving bioflavinoid capsules fared better than the controls. In the whole series, the 71 patients who did not receive bioflavinoid compounds produced 22 surviving infants (a 31% success rate) and the 32 who did receive bioflavinoids produced 24 surviving infants (a 75% success rate). The author concludes by stating that though the results seem striking, the number of treated patients is small, and that further studies are in progress.

Pregnancy Testing in Tranquillized Patients.

J. E. Hodgson (*J. Amer. med. Ass.*, August 15, 1959) has investigated reports that up to 75% false-positive results may occur in pregnancy tests performed on male frogs with urine from non-pregnant patients receiving promazine. The author performed pregnancy tests on 50 patients of both sexes who were taking varying doses of phenothiazine compounds in a psychiatric hospital. With the technique used by the author no strongly positive responses resulted. Serum instead of urine was used in injecting the frogs. Hyaluronidase was injected with the serum to facilitate absorption. Two frogs weighing from 25 to 50 grammes were used for each of the 50 tests, and there was no evidence that the test carried out in this way would give false-positive results in patients receiving tranquillizers.

Carcinoma of the Vulva.

S. Way (*Amer. J. Obstet. Gynec.*, April, 1960) discusses the evolution of the operation of radical vulvectomy in his hands. He compares the results obtained in patients submitted to operation from 1943 to 1949 with the later series of 1949 to 1954, and describes modifications in operative technique developed during the last five years. Poor results in the treatment of carcinoma of the vulva prior to 1939 are considered to be largely due to the rarity of the disease, no single surgeon seeing enough cases either to become proficient in its treatment or to conduct adequate research. The operation developed by the author aims at wide excision of the vulva and total attack on the lymph nodes, leaving the extensive wound open to heal by granulation. Routine dissection of the lymph nodes seemed desirable since nearly half of the patients had node involvement and clinical detection of cancerous involvement was impossible. Analysis of patients treated during 1943 to 1949 was as follows: 79 patients seen; 65 underwent operation (83% operability rate); 61% of all patients seen were alive and well after five years; when lymph nodes were involved 48% survived, and when the nodes were free 86% survived. Five-year results of the second series (1949 to 1954) have not been quite so successful. Ninety-six patients were seen, the operability rate remained the same, but the absolute five-year survival rate dropped to 49%.

However, this second series contained more advanced cases, and an outbreak of virulent staphylococcal infections affected the mortality rate. Of 143 patients operated upon in both series, lymph nodes were involved in 42%; superficial nodes only were involved in 26%, both superficial and deep nodes in 13%, and deep nodes only in 3%. The low incidence of involvement of the deep nodes prompted the author to attempt to assess their state at the time of operation, with a view to curtailing the extensive dissection when not indicated. A technique is described by which a deep node is removed early in the operation and a diagnosis of its condition is made in six minutes. If these deep nodes are normal the inguinal ligament is not divided and further deep node dissection is not performed. If the superficial nodes are obviously involved the deep nodes are always dissected. Lymph nodes were involved in 62% of anaplastic tumours, while differentiated tumours had only a 35% involvement. The author also draws attention to a small group of "giant cell" tumours (five cases), considered to be an unusual type of epithelioma. Patients with this type of tumour have a short history of growth, large tumours, metastases and poor response to treatment. Other operational modifications described by the author are a method of attempting to close the skin wound without sacrificing the extent of excision, and the transplantation of the sartorius muscle to cover the femoral vessels; this serves to protect these vessels and reduce the risk of secondary hæmorrhage. The author considers that the results of these operations have been most gratifying but that the operation is probably but a passing phase in cancer therapy.

Genital Tuberculosis in Women.

A. M. SUTHERLAND (*Amer. J. Obstet. Gynec.*, March, 1960) reports a detailed study of 325 cases of genital tuberculosis in women investigated in Glasgow during the past nine years. The incidence of this disease has been assessed from the following aspects: examination of histological material from a gynæcological hospital gave an incidence of 1·1%; study of the clinical records of the same hospital gave 0·27%; the incidence among infertility patients at this hospital was 5·6%; among patients of all ages with functional uterine bleeding there were 1% with endometrial tuberculosis, and among those aged 20 years and under the incidence was 4%. The author emphasizes the importance of early diagnosis and treatment of endometrial tuberculosis in young patients before the tubes are damaged beyond recovery. A history of previous extragenital tuberculosis was obtained in 177 of the 325 patients studied. A further 77 patients showed radiological or bacteriological evidence of previously unsuspected extragenital infections. The interval between the earlier tuberculous manifestations and the discovery of the genital lesion varied widely, but in the majority it was five years or more. Among 294 married patients in this series, only 38 gave a history of previous pregnancy. It is suggested that about 3% of patients developed a tuberculous lesion during pregnancy or in the post-partum period. The principal symptoms of the disease were: infertility (142), abdominal pain (76), uterine bleeding (48) and amenorrhœa (26). Endometrial involvement was found in 318 patients, the Fallopian tubes were infected in five, and the cervix in two. However, the author considers it is almost certain that the tubes are affected in most, if not all, of the cases of endometrial tuberculosis. The tubes were found to be blocked in 71 of 112 patients investigated. Adnexal swelling, usually bilateral, was detected in 156 patients. Diagnosis was based initially on the histological findings, but bacterial confirmation was sought in 286 patients and obtained on 198 of these. The organism has been typed in 147 cases, and in every case was of the human type. In 38 patients with tuberculous endometritis no treatment was given initially; in none of these did the disease tend to undergo spontaneous cure, and in some treatment was required during the observation year because of clinical deterioration. Drug treatment was given to 293 patients according to one of four methods. (i) Streptomycin and PAS given to 165 patients resulted in arrest or cure in 67% and recurrence after treatment in 21%. (ii) Treatment of 70 patients with streptomycin and isoniazid was followed by recurrence in 13%. (iii) Treatment with PAS and isoniazid (52 patients) is showing encouraging results. (iv) Treatment with isoniazid alone has been abandoned. Eighteen patients in the series were treated surgically, all of whom had first had at least one course of drug therapy. The indications for surgery were persistent abdominal pain, recurrence of endometrial infection after drug treatment and the persistence or development of large adnexal masses after drug treatment. The author considers that the scope of surgery should be enlarged rather than curtailed and that surgery when indicated should be radical, irrespective of the age of the patient. Total hysterectomy and bilateral salpingo-oöphorectomy can usually be performed with relative ease, despite adhesions. No patient developed a post-operative fistula, a relatively common complication before the introduction of preliminary drug treatment. Apart from patients whose primary complaint was infertility, the symptomatic results after drug treatment are considered by the author to be generally satisfactory.

Primary Carcinoma of the Vagina.

G. H. ARRONET *et alii* (*Amer. J. Obstet. Gynec.*, March, 1960) report a study of 25 cases of primary carcinoma of the vagina during the years 1926 to 1958. All were pathologically proved, and the patients had active treatment and have been followed up. The incidence of this condition was 1·2% of all cases of primary malignant disease of the female genital tract. The ages of patients ranged from 35 to 67 years; 22 patients were married, six were nulliparous, 19 had passed the menopause, and six were still menstruating at the time of diagnosis of the tumour. No single factor was noted as a predisposing cause in the series. One patient had worn a rubber ring pessary for years, one patient had extensive vulvo-vaginal varices, one had a procidentia and a Gartner's duct cyst had previously been removed from one patient. The outstanding symptoms of these patients were spontaneous vaginal bleeding, contact bleeding, an obvious swelling noticed by the patient, local pain, and weight loss. The commonest site of the neoplasm was in the upper third of the vagina, situated to one side or on the posterior wall. There were twice as many ulcerative lesions as fungating ones. All tumours were of the epidermoid variety with the exception of one transitional cell carcinoma. Sixteen were anaplastic and six were differentiated. Twenty-four of the 25 patients were treated with radium by a variety of techniques, with or without deep X-ray therapy. One patient was treated by radical surgery. Eleven patients survived for five years; most of these were treated by radium application without additional deep X-ray therapy. Six patients had a recurrence of carcinoma and metastases were found in eight instances. Seven of the eight patients with metastases had involvement of the inguinal glands. Complications due to the neoplasm or its treatment included three recto-vaginal fistulæ and three vesico-vaginal fistulæ. The authors consider that any method of staging of this carcinoma is difficult, but that that described by Courtial is the most satisfactory.

Paget's Disease of the Vulva.

R. H. KAUFMAN *et alii* (*Amer. J. Obstet. Gynec.*, March, 1960) report a case of Paget's disease of the vulva and discuss the lesion after detailed histological examination of the whole vulva. The histological features of this disease, similar to those found in Paget's disease of the nipple, are well known. However, opinion differs as to whether Paget's disease of the vulva represents a primary intraepidermal lesion or whether it is secondary to an underlying apocrine gland carcinoma. No apocrine gland carcinoma was found in this case. The patient was a woman aged 58 years who had borne one child and had complained of pruritus and soreness of the vulva for several months. The vulva was found to be the site of clinical leucoplakia involving both labia majora and labia minora. The skin was tough and leathery and several small areas of superficial ulceration were present. Simple vulvectomy was performed and sections were taken and examined at intervals of less than 1 mm. throughout the entire specimen. The histological picture was one of marked hyperkeratosis and parakeratosis with atypical epithelial hyperplasia. Large irregular "Paget" cells were seen, particularly in the basal layer of the epidermis and infiltrating the full thickness of the epithelium and outer keratinized layer. There has been no recurrence of the condition after three years. The authors consider that it is unlikely that an underlying apocrine gland carcinoma has been missed and that the case is one of primary intraepithelial extramammary Paget's disease. They suggest that cell rests from the primary epithelial germ with apocrine gland potential may be left in the surface epidermis and that these rests may be the source of intraepidermal Paget's disease.

British Medical Association.

VICTORIAN BRANCH: SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held on May 14, 1960, at the Glenelg Base Hospital, Hamilton. The meeting took the form of a series of clinical demonstrations by members of the staff of the hospital.

Hydatid Disease.

MR. S. C. FITZPATRICK showed a male student, aged 28 years, suffering from primary hydatid disease in the body of the third lumbar vertebra. In 1951 the patient had fallen while playing tennis, and later complained of pain in the left groin and in the front and back of the left thigh. In 1953 he was treated as probably suffering from a herniated nucleus pulposus. In 1954 an X-ray examination revealed what was considered to be a compression fracture of the body of the third lumbar vertebra. The condition was later diagnosed as Kummel's disease, and later again as a low-grade infection. The patient was fitted with a spinal support. In 1955 he was treated as suffering from spinal tuberculosis. He was put in a plaster of Paris bed and given full anti-tuberculosis treatment. There was no relief of the pain. In 1956 a tumour was suspected, and at a first operation on March 14 a surgical approach as for lumbar sympathectomy was used. The psoas muscle was found to be bulging, and when it was opened herniated cysts were found and many were removed. The cysts were drained. The patient was nursed in a plaster of Paris bed for six months. Later he was given a spinal support and allowed to walk. The pain was easier for some months and then began again on the right side. On August 17, X-ray examination revealed further destruction of the body of the third lumbar vertebra. In February, 1957, the second lumbar vertebral body was found to be involved. In July, operation was undertaken on the right side through the same type of approach as on the left. The findings were the same as on the left side. Many cysts were present in the right psoas muscle. Drainage was established and the pain was relieved, but it returned if the discharge ceased temporarily. In September, an implantation cyst broke on the left side and the patient's temperature rose to 104° F. He had a severe general reaction (anaphylactic), which subsided in 48 hours. A cultural examination of the discharge yielded a staphylococcus. The result of the Casoni test was positive. There was no enlargement of the liver, and no signs of spinal compression had appeared until then. The pain in the legs was increasing. An X-ray examination of the chest revealed a metastatic cyst in the left lung.

The patient was admitted to Glenelg Base Hospital on October 20, 1958, in good general condition. There was advanced destruction of the bodies of the third and of part of the second lumbar vertebræ. Instability of the lumbar part of the spine was present, and there was a cyst in the left lung. The patient was highly sensitized to hydatid antigen. There were many implanted cysts in both operation areas, and there was a staphylococcal infection of the sinuses.

The following plan of action was laid down: removal of implanted cysts; stabilization of the lumbar part of the spine by Albee's graft; desensitization of the patient to hydatid antigen by a graded series of injections; removal of the primary bony foci in the second and third lumbar vertebræ; removal of the metastatic lung cyst in the lingula; rehabilitation of the patient; the overcoming of intercurrent infections, malaria, sinusitis, gastro-enteritis and staphylococcal osteomyelitis. Mr. Fitzpatrick said that the plan had been carried out. The sinuses had been closed for five months, and the patient had been free from pain during that period. The spine was stable and there was no lumbar curve. He earned his own living on a "work, earn, learn" basis in a Melbourne firm which had a branch in New Delhi, to which he might be able to transfer later. He was full of hope, ambition and the desire to work and study, and was making good use of his opportunities. Mr. Fitzpatrick said that in view of the insidious nature of osseous hydatidosis, he felt it imperative to maintain an attitude of scepticism of a cure for several years.

Cryptogenic Cholangitis.

Mr. Fitzpatrick's second patient was a man, aged 34 years, who on February 4, 1960, had been referred for investigation with fever and lower precordial and epigastric pain, and who was mildly jaundiced. The liver was enlarged to five fingers' breadth below the costal margin. A suppurating hydatid cyst of the liver was suspected. The response to the Casoni test was mildly positive. Laparotomy was performed next day. No hydatid cyst, but multilobular hyperplasia of the liver was found. A section of the liver was taken for biopsy, and the pathologist reported the following findings: multilobular hyperplasia; little fibrosis; some bile duct hyperplasia which might in fact represent crowding of ducts left behind after previous lobular collapse; healthy parenchymal liver cells with no fatty change. The pathologist commented that the picture was suggestive of liver regeneration after hepatitis rather than of ordinary portal cirrhosis. However, he could not completely exclude cirrhosis of nutritional or alcoholic origin.

For 10 days after operation the patient's condition was much improved and he remained afebrile. His temperature then rose again, and despite intensive therapy with "Tetracyn", chloramphenicol and sulphonamide drugs, remained high for the next three weeks. During all that time he was having rigors and drenching sweats. His spleen became palpable. A number of investigations were carried out, and the following findings were obtained. A blood examination showed a falling hæmoglobin value to 82% and a leucocyte count of 20,370 per cubic millimetre, of which 83% were polymorphs. A blood culture produced a negative result. Microscopic examination of fæces revealed no amœbæ or parasites. The cephaline flocculation test produced a negative result. The total serum protein content was 5·1 grammes per 100 millilitres (albumin 1·5 grammes, globulin 1·6 grammes, gamma globulin 1·0 grammes). The serum alkaline phosphatase content was 14 King-Armstrong units per 100 millilitres. The serum bilirubin content was 1·4 milligrammes per 100 millilitres. The zinc-sulphate turbidity was 4 units.

On February 27, treatment with "Deltastab" in a dosage of 15 milligrammes every six hours was begun, and the temperature fell. Two days later it rose again, and since by that time the patient's progress was beginning to look doubtful, he was transferred to Prince Henry's Hospital, Melbourne, under the care of Dr. I. Epstein. The patient was extensively investigated with the following results. A full blood examination showed that the hæmoglobin value was 76%, the leucocytes numbered 22,000 per cubic millimetre (myelocytes 1100) and in a blood film mild anisocytosis affecting the erythrocytes and an occasional polychromatic form were evident. There was neutrophilia with a pronounced shift to the left, and many cells contained toxic granules. Platelets were plentiful. Liver function tests gave the following results. The total serum protein content was 6·9 grammes per 100 millilitres (albumin 3·4 grammes, globulin 3·5 grammes), the bilirubin content was 0·5 gramme per 100 millilitres, the serum alkaline phosphatase content was 30 units, and the gamma globulin was 9 units. The cephalin flocculin test produced a "+++" reaction. A Mantoux test with 1:1000 old tuberculin produced a negative result, and an agglutination test produced a negative result. X-ray examination of the chest including fluoroscopic screening of the diaphragm revealed no abnormality. Blood cultures gave normal results. The erythrocyte sedimentation was 56 millimetres in one hour (Wintrobe). A Wassermann test produced a negative reaction. A bone marrow biopsy revealed a mild increase in the leucocyte series, but no other abnormality. The prothrombin time was 100%.

During the patient's stay in Prince Henry's Hospital his temperature kept on swinging, going as high as 41·2° C. No specific treatment was given at first. Later he was given a course of emetine to exclude the possibility of amœbiasis. It made no difference to the temperature. Laparotomy was performed on March 17. The liver was found to be enlarged and cirrhotic, and a chain of grossly enlarged lymph nodes was present in the para-aortic region. Biopsy specimens were taken from both the liver and the glands. The latter specimen showed intense non-specific hyperplasia and sinus catarrh, the former showing moderate cirrhosis, and the abundance of polymorphs in the portal tract was indicative of suppurative cholangitis.

Mr. Fitzpatrick commented that the first liver biopsy done in Hamilton revealed cirrhosis, but no cholangitis. Before operation the patient was given steroid therapy as a routine procedure, and after operation penicillin and streptomycin therapy was commenced by the surgeon. Steroid therapy was continued. On the second day after operation his temperature fell to normal. "Achromycin" was given from the seventh day after operation, and penicillin and streptomycin were stopped. Prednisolone was stopped on April 30, and the patient's temperature had remained about 37·5° C. The report from Prince Henry's Hospital was that he had improved greatly, was eating well and was up. They were surprised at his improvement, but still did not

know the ætiology of the suppurative cholangitis and cirrhosis of the liver. Another liver biopsy specimen was taken on April 4. Culture of the specimen produced no growth of pathogens. Examination of a section revealed chronic or subacute hepatitis, with evidence of some degree of resolution of associated suppurative cholangitis. Another series of investigations gave the following results. The erythrocyte sedimentation rate was 40 millimetres in one hour. A full blood examination gave the following findings: hæmoglobin value 91% (13·2 grammes per millilitre), leucocytes 2200 per cubic millimetre (neutrophils 14,600 per cubic millimetre). Liver function tests gave the following results: total serum protein content 6·8 grammes per 100 millilitres (albumin 3·4 grammes, globulin 3·4 grammes), bilirubin 0·3 milligramme per 100 millilitres, serum alkaline phosphatase 16 units, gamma globulin 11 units, cephalin flocculation test a "+" reaction. The patient was sent home from Prince Henry's Hospital on a dosage of 0·5 gramme of "Achromycin" four times a day for two weeks, to be followed by 250 milligrammes a day for another two weeks, and he was to be readmitted later, so that another liver biopsy could be performed.

Dystrophia Myotonica.

DR. C. E. SAWREY showed a male patient, aged 44 years, who said that for about 20 years after a severe attack of pleurisy and pneumonia he had noticed weakness starting in his arm and gradually affecting the rest of his body. On examination of the patient the gross wasting of the muscles could be seen, the sterno-mastoids and forearms being characteristically severely involved. The slow relaxation of the muscles was not so obvious, but he had difficulty in releasing a hand-grasp. The associated feature of frontal baldness was present. Cataracts could not be detected, but there appeared to be mild testicular atrophy.

Fracture of the Humerus.

MR. A. D. MATHIESON showed a boy, aged 11 years, who had been admitted to hospital on January 5, 1960, with the history that he had fallen from a horse and sustained an oblique fracture of the left humerus. There was a fair amount of swelling in the left shoulder region. The arm was maintained in abduction and external rotation. Manipulations were carried out, but no satisfactory reduction of the fracture was obtained.

Operation was undertaken on January 21, through a Henry shoulder incision. The distal fragment was found displaced upwards and laterally, with interposition of muscle between the ends of the bone. Reduction of the fracture was carried out. The most satisfactory position for maintaining the fragments in position was with the arm abducted, the elbow flexed and the arm lying across the chest. A Steinmann pin was introduced backwards through the upper fragment to emerge near the greater tuberosity. The overlying skin was incised and an intramedullary V nail was introduced from above. The Steinmann pin was used as guide. The pin was then removed, and the nail was driven across the fracture line into the medullary cavity of the distal fragment. A check X-ray examination was made to confirm the position of the fragments and the nail. After operation the arm was lightly bandaged to the chest, the elbow flexed to a right angle and supported in a sling. The patient was discharged from hospital on January 30. He was admitted again on March 2, and operated on the next day for removal of the intramedullary nail, being finally discharged on March 5.

Rupture of the Uterus.

DR. C. F. MACDONALD showed a married woman, aged 40 years, who had had eight previous pregnancies. The heaviest child at birth, the sixth, had weighed 8 lb. 9 oz. All the labours except the last had been normal. The last pregnancy in October, 1956, had been complicated by hypertension. When the patient was 39 weeks pregnant, an attempt was made to induce labour by artificial rupture of the membranes, but labour did not ensue, and 36 hours after that procedure the pulsating cord was found lying in the bed. A lower uterine segment Cæsarean section was performed, and a live female child weighing 7 lb. 14 oz. was delivered. The puerperium was uncomplicated. On the evening of the first day the patient's temperature was 100·4° F., but thereafter was never above 98·6° F.

The present pregnancy was as follows. The last normal menstrual period had occurred on May 21, 1959, and the estimated date of delivery was February 29, 1960. At the patient's first visit on September 8, she was 16 weeks pregnant, her weight being 12 st. 12 lb. Her blood pressure was 170/110 mm. of mercury, and the uterus corresponded in size to the period of amenorrhœa. She was given a reducing diet. She continued to attend regularly. The weight gain was well controlled; throughout the entire pregnancy she gained only 14 lb. At no time was there œdema or albuminuria. Her blood pressure fluctuated between 160/100 and 145/95 mm. of mercury. When she was 36 weeks pregnant there was a reading of 160/110 mm. of mercury, and she was given "Serpasil" in a dosage of 0·25 milligramme three times per day. Throughout the last six weeks of the pregnancy, the presenting part of the head remained high and fairly mobile above the pelvic brim. On March 1, the pregnancy had reached term and the blood pressure was 160/100 mm. of mercury. The head, though high, was fixed, but not engaged. It was considered unwise to allow the patient to go beyond term with her elevated blood pressure, so she was admitted to hospital and artificial rupture of the membranes was performed. At that procedure the cervix was found to be soft and partly taken up, and the os was dilated to admit two fingers. No pituitary extracts were given, owing to the presence of a scar in the uterus. There were no contractions for 18 hours; mild contractions then occurred and gradually increased in frequency and duration. After eight hours of labour, the patient was becoming distressed, and complained of severe suprapubic pain. Her pulse rate had risen from 80 to 96 per minute. Despite the contractions, there had been no descent in the presenting part and the patient was quite tender in the suprapubic area. The fœtal heart rate was 140 per minute. With those signs of pending rupture of the uterus, Cæsarean section was decided upon. In the thirty-minute interval between the making of that decision and the getting of the patient on to the operating table, a distinct alteration in the contour of the abdomen was noted. A sulcus had appeared between the fundus and the suprapubic region. When the abdomen was opened, an incomplete rupture of the lower uterine segment was obvious. The peritoneum over the lower segment was intact, but meconium-stained liquor, blood and fœtal parts were visible behind the peritoneum. The child was extracted alive, and weighed 6 lb. 15 oz. The placenta was placed on the interior wall of the uterus, and its lower margin appeared to overlap the upper edge of the uterine tear. When the placenta, blood and meconium were mopped away, an extensive tear in the lower segment was found, and of even more importance, the end of the self-retaining catheter was visible, indicating that the tear had extended into the bladder. The irregular hole in the bladder was approximately three inches long. With the assistance of Mr. Fitzpatrick, a total hysterectomy was performed and the bladder was repaired with continuous "00" catgut sutures to the mucosa and interrupted sutures to the muscle and adventitia. Intravenous therapy and continuous bladder drainage were given.

Proteinuria in Siblings.

DR. J. V. RYMER showed a youth, aged 16 years, who in 1958 had been examined for life insurance with a satisfactory result. His blood pressure was then 120/80 mm. of mercury. His urine contained albumin. Examination of the optic fundi revealed bilateral temporal optic atrophy. Microscopic investigations of the urine revealed an occasional epithelial cell. Renal function tests gave the following results: (i) Three consecutive early morning specimens of urine were examined. The first had a specific gravity of 1024 and contained "++" albumin. The second had a specific gravity of 1026 and contained "+" albumin. The third had a specific gravity of 1022 and contained "+" albumin. (ii) A Fishberg concentration test gave the following findings. At 8 a.m., a specimen of 3 oz. of urine had a specific gravity of 1006. At 9 a.m., 23 oz. of urine had a specific gravity of 1002. At 10 a.m., no urine was passed. (iii) A urea clearance test gave the following results. The urinary output rate was 0·71 ml. per minute. The urinary urea content was 1650 mg. per 100 ml. The blood urea content was 20 mg. per 100 ml. The standard clearance was 108% of average normal clearance. (iv) An electrophoretic pattern showed the total serum protein content to be 7·19 mg. per 100 ml., distributed as follows: albumin 40·2%, alpha-1 globulin 5·1%, alpha-2 globulin 12·5%, beta globulin 16·6%, gamma globulin 25·6%. It was considered that no renal deficiency was present. In 1960, the patient was perfectly well and had no headaches, and general physical examination gave satisfactory results. His blood pressure was 140/90 mm. of mercury, his urine contained some albumin, and bilateral temporal optic atrophy was noted. Laboratory investigations included a microscopic examination of the urine, which revealed an occasional epithelial cell, a moderate number of granular casts and an occasional hyaline cast. The patient was referred to the Clinical Research Unit of the Royal Melbourne Hospital.

The patient's elder brother, aged 19 years, had been examined in 1954 on account of recurrent frontal headaches. General physical examination revealed no abnormality. His blood pressure was 120/80 mm. of mercury, and his urine contained a heavy cloud of albumin. Examination of the optic fundi revealed bilateral temporal optic atrophy. Microscopic investigation of the urine revealed numerous casts and a few erythrocytes. Renal function tests gave the following results: (i) the urea concentration test — first hour 1·8%, second hour 2·0%, third hour 2·3%; (ii) the urea clearance test—first hour 42% of normal, second hour 38% of normal, average 40% of normal function; blood urea content 12 mg. per 100 ml. It was considered that there was definite evidence of renal deficiency. In 1960, the patient suddenly presented himself with severe headache, nausea, vomiting, dizziness, nocturia and frequency of micturition. On examination of the patient, his blood pressure was found to be 220/130 mm. of mercury. Bilateral temporal optic atrophy was present, with exudates, hæmorrhages and slight œdema of the nasal edges of the optic discs. He was referred to the Clinical Research Unit of the Royal Melbourne Hospital. Microscopic investigation of the urine revealed granular casts, occasional pus cells and erythrocytes. Renal function tests gave the following findings: (i) urea clearance, 50% of normal; (ii) blood urea content, 66 mg. per 100 ml.; (iii) serum cholesterol content, 265 to 337 milligrammes per 100 millilitres; (iv) serum lipid content, 1797 to 3197 mg. per 100 millilitres. Intravenous pyelography revealed poor renal excretion in both kidneys. Renal biopsy showed patchy glomerular hyaline change and hyalinization of the interlobular arteries. It was considered that renal vascular disease was present, and also probably chronic pyelonephritis or glomerular nephritis. The patient's condition was discussed at a clinical meeting with Professor McMichael and Professor Alexander. Opinions differed as to the underlying renal lesion and the prognosis. Treatment had been by the administration of "Mevasine" in the dosage of 0·5 mg. three times a day, reserpine 0·5 mg. three times per day, and chlorothiazide 0·5 gramme twice a day.

Hydatid Disease in the Biliary Tract.

DR. A. M. MARSHALL showed a child, aged 12 years, who had first been examined in September, 1955, at the age of seven years, with the complaint of cough, present for several days, and of loss of appetite. The father was a station hand at Harrow, and the patient was the eldest of three children. There was no tuberculosis or other illness. The child had had several attacks of tonsillitis. On examination, the patient was seen to be a thin child with a loose cough. The temperature was 101° F., and the pulse rate 80 per minute. The tonsils were enlarged, and râles were present in both lungs. The heart sounds were regular and clear. The liver was enlarged. No other abnormalities were detected. The patient was receiving antibiotic therapy. The Casoni test produced a negative result. The urine was normal. In October the patient was admitted to hospital, having been suffering from pneumonia for two weeks. A further check was made after the child's discharge from hospital, and tonsillectomy was arranged. In November the tonsils and adenoids were removed. The patient was next examined in April, 1956, having had a chest infection. X-ray examination revealed no essential change. The patient was examined by a private doctor in Ausust, 1956, who noted an enlargement of the liver. On examination at the hospital, the child was found to have a productive cough, abdominal pain and vomiting of one week's duration, and was not gaining any weight. On examination of the patient, râles were present on the left side of the chest, the temperature was 100° F. and the urine was normal. The child was admitted to the Base Hospital. The condition cleared under therapy with antibiotics and postural drainage. In July, 1958, the family was living in Hamilton, and the child suffered from mumps and vomiting. He was examined by a doctor and diagnosed as suffering from undescended testes. Hormone therapy was instituted. The next day vomiting, oliguria and hepatomegaly were present, and the boy was admitted to the Base Hospital for investigation. The Casoni test was repeated and gave a positive result. A review of the situation by Mr. Fitzpatrick resulted in a request for sieving of stools, and what appeared to be a cyst membrane was isolated. In September, 1958, a hydatid cyst of the bile duct was removed, and this was followed by laparotomy and a cholangiographic examination while the patient was on the operating table. In February, 1959, the boy came for a pre-school check. No hepatomegaly and no icterus were present, and it was agreed that the child should be examined every six months.

Out of the Past.

RULES FOR THE GUIDANCE OF THE RESIDENT MEDICAL OFFICER.

[Melbourne Hospital, 1854.]

1.—The Resident Medical Officer shall live in the house, and shall not leave it, except on necessary occasions; he shall not be absent for more than three hours at any one time, nor after twelve o'clock at night, without the sanction of the Committee of Management.

2.—He shall have the charge of the patients during the absence of the Physicians and Surgeons, and shall report to the Committee of Management, at its next meeting, any patients who may have been irregular or disorderly.

3.—He shall have the immediate superintendence of the wardsmen and nurses, and shall preserve order and sobriety in the establishment; and in any case of insubordination, or gross default of duty, on the part of any wardsman or nurse, he shall discharge such servant, and, if necessary, shall hire a substitute for such servant discharged; and he shall report his having done so, with the cause of such discharge, to the Committee of Management at the next meeting.

4.—He shall have the charge of, and be accountable for, the medicines and medical instruments; and shall make an inventory of the same in a book to be kept for that purpose, in which he shall regularly enter the receipt of each article; and he shall, on the last day of the months of March, June, September and December of each year prepare and submit to the Committee of Management a list of medicines and medical instruments required for his department during the ensuing quarter.

5.—He shall enter regularly in proper books, to be kept for such purposes, the names of the patients as they are admitted and discharged, and note, if required, the nature and history of their diseases whilst in the Hospital; the receipt, issue, expenditure, loss, or breakage of medicines, medical instruments, and other things in his charge, and shall have such books ready at all times for the inspection of the Committee of Management.

6.—He shall accompany the Physicians and Surgeons every day through the wards, and report to them the state of the patients, and shall enter in a book to be kept for that purpose the prescriptions of the Physicians and Surgeons.

7.—He shall also visit each patient every morning and evening, and enquire if the treatment prescribed has been attended to, and if any cause of complaint exists; and should any patient have any complaint to prefer, he shall enter the same in the Patients' Complaint Book immediately, in the presence of the wardsman or nurse of the ward, and shall lay such book before the Committee of Management at each meeting.

8.—He shall, on his visits to the wards, examine their condition with respect to cleanliness, temperature, and ventilation, and observe if the wardsmen and nurses have done their duty.

9.—He shall affix to the bed of each patient, his name, age, disease, the date of his admission, the name of the Governor by whom he has been recommended, and the diet ordered by the Medical Officer.

10.—He shall perform all the minor operations of surgery, and the post-mortem examinations, not personally performed by the Physicians or Surgeons.

11.—In the absence of the Physicians or Surgeons, in all cases of emergency, he shall cause immediate notice of such emergency to be given to them; being authorised, in the meantime, to act to the best of his judgement, avoiding, as far as possible, any unnecessary interference with the duties of these officers; and, when interfering, he shall make a full entry of the particulars of such interference in the Case Book.

12.—He shall report those patients that are absent, irregular, or disorderly to the Physicians and Surgeons, who shall have power to dismiss any patient guilty of gross misconduct.

13.—He shall not, on any pretence whatever, be concerned in any medical or surgical practice out of the Hospital, nor in any other business; nor shall he divulge any of the proceedings of the Committee or Medical Officers in the discharge of their duties.

14.—He shall give due notice to all the Physicians and Surgeons as often as a consultation is to be held, or an operation performed.

15.—He shall see that the patients do not partake of any food, liquor, or medicine except that prescribed.

16.—He shall procure such articles as may be required in small quantities for his own department during the week; but he shall not in any case purchase any article for the Hospital exceeding in value £2, or enter into any contract on account of the Hospital, exceeding that sum in amount, without an order from the Committee of Management, or a special order signed by the Physician or Surgeon by whose direction the article has been ordered, or contract entered into; and in the latter instances he shall lay such special order before the Committee of Management at its next meeting.

Medical Societies.

PÆDIATRIC SOCIETY OF VICTORIA.

A MEETING of the Pædiatric Society of Victoria was held on December 9, 1959, at the Royal Children's Hospital, Melbourne.

Duplication of the Upper Part of the Urinary Tract.

MR. D. LENAGHAN discussed duplication of the upper part of the urinary tract. He said that two main types of double ureters existed. In one, the double ureters were complete and there were two separate orifices. In the second type, the double ureters were incomplete, and joined to form a common stem, so that there was only one orifice and that was in the normal position in the bladder. In complete double ureters, one ureteric orifice was normally placed at the lateral margin of the trigone, and the other orifice might open in the bladder, urethra or vagina in descending order of frequency. Rarely it opened into the genital tract—for example, into the ejaculatory duct or seminal vesicle. The ureter of the ectopic orifice was always attached to the upper portion of the kidney, while the middle and lower groups of calyces were drained by the ureter with the normally situated orifice. Mr. Lenaghan then discussed the role of double ureters as a cause of symptoms in children. He said that the symptoms commonly produced were incontinence of urine and similar symptoms, those due to urinary tract infection, and recurrent abdominal pain.

The main causes of urinary incontinence were ectopic ureteric orifices, certain types of neurogenic bladder, such as that due to myelomeningocele, and functional disturbances in which there was poor control without any demonstrable organic lesion. Ectopic orifices were a very rare cause of incontinence. Only those located in the distal part of the female urethra or vagina were capable of causing it. In the male, ectopic orifices did not occur below the verumontanum, below which the urthera still retained important sphincteric action. Thus, incontinence due to this cause was not seen in male children. The clinical features of incontinence due to an ectopic ureteric orifice was constant visible wetness in a female child in whom normal micturition also occurred, the bladder being impalpable; the leaking orifice might be able to be seen in the neighbourhood of the urethra or vagina. Intravenous pyelography might give useful information. A double ureter might be seen, with the ectopic ureter dilated because of partial obstruction in the submucosal part of the urethra owing to pressure from the urethral sphincter. If the ectopic portion of the kidney was found to be non-functioning on intravenous pyelography, its presence might be suspected if the kidney shadow was larger than that outlined by the calyces, or if the upper calyx was absent, or if the lower calyces were displaced laterally. Incontinence due to a neurogenic bladder was differentiated by the presence of spina bifida and an expressible bladder, or a firm, non-tender, palpable bladder with overflow.

Incontinence from functional causes was not true incontinence, but consisted of poor control, and frequency and precipitancy of micturition and sometimes scalding. In moments of excitement, the child lost control. There might be nervous symptoms as well. Because of similar symptoms, urinary tract infection should always be excluded; but the finding of a double ureter in those cases was incidental.

The criterion for diagnosing urinary tract infection was the recognition or culture of organisms from a specimen of urine collected under sterile conditions. Investigation of those cases might reveal double ureters. If the double ureters were complete, with both orifices opening into the bladder, and if the ureters were of normal calibre, it was unlikely that they were causing infection. Certain types of double ureters predisposed to urinary tract infection by causing stasis. There were three ways in which they could do that. The first was by the production of obstruction. If the ectopic orifice was stenotic or if it opened into the upper part of the urethra, there was obstruction and dilatation of that ureter. Enlargement of the ectopic ureter might then cause secondary obstruction to the normal ureter. The second way in which stasis could be caused was by reverse flow in conjoined double ureters. That type of abnormality was associated with a high incidence of urinary infection. Investigation of those ureters showed delay in emptying due to asynchronous peristalsis, which produced a side flow of urine from one part of the Y-shaped ureter to the other. The emptying time was more delayed if the ureters were dilated. Thirdly, stasis could be caused by vesico-ureteric reflux, which might occur in one or both of the ureters of a double-ureter system. Reflux of that type produced delayed and incomplete emptying, which predisposed the subject to infection. Reflux of sufficient amount to be important could be detected clinically by the double micturition test.

The investigation of puzzling abdominal pains in children might reveal a double ureter. The pain was related to that anomaly only if it was localized to the side of the double ureters, if urinary infection was present and if investigation of the double ureters showed one of the causes of stasis described earlier. Pain was related to double ureters only through the urinary infection to which certain double ureters predisposed. It had been suggested that in conjoined double ureters, disordered peristalsis might cause pain. In the cases reviewed, however, pain and infection always coexisted. In children, vague central abdominal pains were sometimes encountered which might be associated with nervous symptoms, including urinary manifestations such as frequency of micturition. When investigations disclosed a double ureter, that discovery was incidental, unless the double ureter was of a type which produced stasis. Mr. Lenaghan concluded by reiterating that double ureters produced incontinence only if the ectopic ureter opened in the lower part of the urethra or distally in the female; that double ureters predisposed to infection only when they caused stasis; and that pain associated with double ureters was due to urinary tract infection.

MR. L. MURPHY asked whether stasis was always associated with dilatation.

Mr. Lenaghan replied that although stasis was more likely when dilatation was present, it could occur without dilatation —for example, in cases of vesico-ureteric reflux. In conjoined ureters, delayed emptying also definitely occurred, despite the absence of dilatation.

Acrodermatitis Enteropathica.

DR. R. KELLY presented the clinical details of a boy, aged eight years, suffering from acrodermatitis enteropathica.

DR. CHARLOTTE ANDERSON then discussed the biochemical investigation and management of the patient.

The boy showed the typical skin manifestations of the disease, together with complete loss of hair from all parts of the body, and loss of finger-nails and toe-nails. The symptoms had been present since the age of nine months. He had also had abnormally frequent and loose bowel actions since then, and was undersized. Investigations of the gastro-intestinal tract had revealed mild steatorrhœa, and some reduction in the concentration of trypsin, lipase and amylase in the duodenal aspirate. A trial of a gluten-free diet had failed to produce improvement in his skin condition; but within a week of commencing "Diodoquin" therapy there had been considerable improvement, and within one month hair was growing on the scalp and the rash had disappeared. The boy had been kept on "Diodoquin" in a dosage of 1500 mg. per day for the past three years, and with that he had no skin lesion, there was normal growth of body hair, stools and intestinal absorption were normal, and he was growing. During upper respiratory infections he might need some increase in the dosage of "Diodoquin", and if the tablets were ceased skin lesions reappeared.

DR. KATE CAMPBELL asked whether those cases always appeared at the time of weaning, and whether the removal of cow's milk was helpful.

Dr. Anderson replied that that was not so.

DR. H. BREIDAHL asked whether "Diodoquin" was absorbed from the bowel. "Enterovioform", a related drug, certainly was absorbed.

Dr. Anderson replied that "Diodoquin" was absorbed, but less so than "Enterovioform".

DR. M. ROBINSON asked whether the parathyroids were involved, as the syndrome presented some resemblances to hypoparathyroidism.

Dr. Anderson replied that the child had had a normal serum electrolyte pattern, but that no specific work had been done on the metabolism of calcium and phosphorus.

Correspondence.

AMNIOCENTESIS IN RH-IMMUNIZED MOTHERS.

SIR: I read with interest the report of Dr. E. Mackay's paper on "Amniocentesis in Rh-Immunized Mothers" (MED. J. AUST., September 17, 1960, page 474).

We have been carrying out a similar study at King George V Hospital for the past two years, and our over-all findings are in agreement with those of Bevis, Walker, and now the Melbourne series. However, our routine differs somewhat from that of the Royal Women's Hospital, Melbourne.

I feel it is important that the first amniocentesis in sensitized women be carried out not later than the thirtieth week of pregnancy, and amniocentesis may be repeated as frequently as weekly. By this means we have been able to save several babies, which were induced or were delivered by Cæsarean section at 32 weeks. True, these babies are very premature and run the risks of extreme prematurity; but to leave such severely affected infants in the uterus to 34 weeks or more means death in utero or the birth of an hydropic baby, who dies despite exchange transfusion.

I do not feel that amniocentesis will be of great help in the assessment of patients referred late in pregnancy. We have found interpretation of fluid taken from such patients difficult and often misleading, and several errors of interpretation have occurred in our series.

A preliminary report of the King George V series will be published in your journal in the near future.

Yours, etc.,

185 Macquarie Street, Sydney. WILFRED CARY.

September 23, 1960.

SPINAL CORD OF NEONATE WITHDRAWN INTACT AT AUTOPSY.

SIR: The brain of the new-born infant is jelly-like and almost diffluent with the exception of the medulla and to a less extent the pons. The latter are firmer and white, evidently from early medullation. In the case now reported, on pulling on the medulla, to my astonishment the whole of the spinal cord down to the lumbar enlargement came away with it, being sufficiently firm to project like a rod with a flattened end. No attachment to it of nerves could been seen, but on opening the spinal canal the cauda equina was found spread out on the dura.

The infant was a male, aged nine days, and weighing 5 lb. 8 oz. Its length was 20 inches. Delivery had been normal. Pyrexia developed with difficulty in respiration followed by sudden deterioration and death. The autopsy, No. 30/57 Queen Victoria Maternity Hospital, Adelaide, showed hæmorrhagic disintegration of much of the left frontal lobe of the brain and less so of the right, the lungs being plum-coloured and airless for about half of their extent. The body had been in the refrigerator apparently for about 30 hours, evidently long enough, in spite of the cold, to allow of autolysis of the nerve roots sufficient to shear them off from the cord when slight traction was applied.

Since this experience, I have held many infants up by the heels and shaken them whilst pulling gently on the medulla and pons in the hope of meeting with other examples. In one instance, a considerable portion of the spinal cord was withdrawn before it parted in the middle.

The interesting thing is that the nerve roots at their attachment are evidently so delicate that a little post-mortem autolysis may cause them to give way throughout the cord. Is it possible that in places during life one or more nerve roots may be sheared off? With this in view, I submitted the above notes to Dr. Trevor Dinning. With his permission, I quote his reply.

I have been through the literature on birth injuries of the spinal cord, and I can find no reference to this phenomenon occurring as a clinical entity. Most of the cases of cord injury have been associated with difficult breech delivery, and this usually results in disruption of the cord in the cervico-thoracic region.

Edith Potter mentions this condition on page 96 of her book "Pathology of the Fœtus and New Born", referring to it as a nerveless cord. She apparently considers that the condition has no pathological significance and is due to post-mortem changes.

Having regard to the differing embryological derivation of the nerve roots and root ganglia on the one hand and the spinal cord on the other, the phenomenon might be regarded as a manifestation of a biological weakness at the junction of the two tissues.

Dr. Edith Potter's description is as follows:

> 'At autopsy, after the brain is freed from its local attachments it may be lifted from the skull and with gentle traction the cord may be extracted from the spinal canal, the nerves being sheared off and left behind. This has been described as a nerveless cord, but it is of no significance and is only the result of an artefact caused by the method of its removal.

Yours, etc.,

University of Adelaide. J. B. CLELAND.

September 22, 1960.

DOCTORS AND THE BLOOD BANK.

SIR: Whilst repaying a "blood debt" to the Red Cross Blood Bank, I was shocked by the following gossip from the receiving "teller". She stated that in 20,000 consecutive deposits, she had only seen two Melbourne doctors giving regular donations to the Mobile Blood Bank.

When my actual overdraft is cleared, my aim is to clear my conscience of one pint of blood I remember spilling as a resident; of several pints that I misjudged the need for, but used because they had been ordered; and of several others allowed to over-age in hospital refrigerators. Later I aim to establish a credit against future use. For any doctor whose conscience is touched by this, a Mobile Blood Bank calls regularly to all suburban and country areas of Victoria (and probably other States). Attendance times can be arranged to fit in with surgeries and an excellent example set to local people.

Yours, etc.,

Moorabbin Clinic, 326A South Road, Moorabbin, Victoria. B. ERREY.

September 22, 1960.

GENERAL PHARMACEUTICAL BENEFITS.

SIR: The world trend towards organized health services has gained considerable momentum in the last two decades. We must face the fact that the pawl has clicked into the ratchet in the development of various public health schemes, propounded, implemented and policed at the Federal Government level in this country. Thus we have become involved in obeying regulations which have been designed to ensure that the Government's plans are carried out with as little waste of public money as possible. These decrees are distasteful and wearisome to many of us. One of our most recent excursions into nationalized medicine—the Pharmaceutical Benefits Scheme—is in its infancy, and, no doubt, amendments and improvements will duly be made.

The purpose of this letter is to criticize the attitude of Dr. E. S. Stuckey, whom I know to be a sincere and intelligent doctor, and one who has given up much of his time to B.M.A. and other activities, related to the welfare of the profession. It is probably this long association with politics that induced him to have published such expressions as: "The profession should insist"; "that the only type of scheme which the profession is willing to administer on the Goverment's behalf"; "let us unite in fighting for professional freedom".

I am almost entirely in agreement with Dr. Stuckey's ideas about improvements in the scheme, but criticize his apparent failure to bear in mind the Government's purpose in introducing the Scheme—namely, to lighten the individual's economic burden of sickness as far as is compatible

with the budget. This type of Government action is, as I have stated, in line with world pattern, and inevitable.

For some unexplained reason, the profession lost the chance to discuss and possibly have modified the Pharmaceutical Benefits Scheme before it was promulgated. If our representatives on the Federal Council maintain effective liaison with the Federal Government, no doubt the Government's objectives can be achieved with the minimum of pinpricks to ourselves. We lose dignity and display a lack of discipline, such as one normally associates with a militant union, by publishing letters like that of Dr. Stuckey.

By all means, let us influence our local councils so they will impress our views on Federal Council, and let us hope that they will be more effective, in future, in persuading Government that our views are the right ones, not for ourselves alone, but for the people as a whole. This, to my mind, is entirely different from threats of non-cooperation in carrying out the laws of the land.

Yours, etc.,

8 Bennett Street,
Cremorne,
New South Wales.
September 25, 1960.

CLIVE H. SELBY.

A REQUEST.

SIR: There appeared on page 90 of *The Speculum*, Number 137, of December, 1935, an article entitled "The Mammalian Ancestry of Man". It was written anonymously under the pseudonym of "Neo-Darwinian". If any of your readers knows the identity of the author, I would be grateful if they would let me know.

Yours, etc.,

366 Church Street,
Richmond, E.1,
Victoria.
September 24, 1960.

BARRY E. CHRISTOPHERS.

Medical Matters in Parliament.

HOUSE OF REPRESENTATIVES.

THE following extracts from *Hansard* relate to the proceedings of the House of Representatives.

August 16, 1960.

Drugs.

MR. WARD asked the Minister for Health, upon notice:

1. Did Mr. J. D. Button, Stipendiary Magistrate, when presiding recently at an inquest into the death of a Canberra resident, find that the deceased died from poisoning resulting from the taking of tablets sold commercially as "Relaxa-Tabs"?

2. Has Mr. Button recommended that the Commonwealth Director-General of Health should have this product placed on the restricted list so that it would be supplied only on production of a doctor's prescription?

3. Was a recommendation also made by Mr. Button that the State Directors of Health be asked to take similar action in their respective States?

4. Are any previous cases of death, attributable to the taking of these tablets, known to his Department?

5. Is any action to be taken as a result of Mr. Button's recommendations; if so, what are the details?

DR. DONALD CAMERON: The answers to the honorable member's questions are as follows:

1. Yes.

2. Yes.

3. Yes.

4. Individual medical officers of the Department of Health have become aware of a number of cases of death from poisoning resulting from the taking of excess quantities of drugs of this kind.

5. Prior to Mr. Button's recommendation action had already been commenced to have an amendment made to the Australian Capital Territory Poisons and Dangerous Drugs Ordinance with a view to restricting the supply of two of the main constituents of these tablets to persons who present doctor's prescriptions. Queensland State law already contains provisions to this effect. The question of amending the law in States other than Queensland is under examination by the appropriate State authorities.

August 17, 1960.

Hospital Benefits.

MR. HAYLEN: In asking the Minister for Health a question I should like to direct his attention to what I am informed by constituents is a rather miserable practice in relation to the hospital contributions scheme, whereby the contributions of people of the age of 65 are put into a special account and special privileges are taken from them without their being informed. In fact, if they have been paying 3s. a week for years, when they reach the age of 65 the fund transfers them to special account. Thereafter, if they enter a private hospital which is not registered as a private hospital, they are mulct of the full charge and get no compensation. Is there any way in which the Minister can speak to the organizations about this and see whether he can answer the questions about the position that I receive from my constituents?

DR. DONALD CAMERON: When the special account procedure was introduced in this House I gave a very full explanation of the way in which it worked, which made it quite plain that nobody was disadvantaged by it but that many people acquired additional advantage from it. What actually happens when people attain the age of 65 is that they are transferred to special account.

MR. HAYLEN: Be not so advised.

DR. DONALD CAMERON: It is quite common knowledge that they are transferred to special account. But if they are insured under any particular fund to which they are contributors and incur expenses of that order they are still paid those expenses.

MR. WARD: They are not!

MR. SPEAKER: Order! the honorable member will refrain from interjecting.

DR. DONALD CAMERON: The honorable member for East Sydney says that they are not. That is quite untrue. If a contributor who is insured under any particular table enters hospital and receives a bill from the hospital, he is paid the full amount for which he is insured unless that amount is in excess of the hospital charge. Before the institution of the special account system it was frequently the lot of a contributor to be paid no fund benefit at all because the funds could, and did, refuse to recognize many hospitals. In fact, what has happened to the special account contributor is that he is better off and no worse off than he was before.

August 23, 1960.

Therapeutic Substances.

MR. WHITLAM asked the Minister for Health, upon notice:

1. On what dates have the Therapeutic Substances Advisory Committee and the Biological Products Standards Committee met in 1959 and 1960?

2. Is it proposed to appoint the Therapeutic Substances Standards Committee as provided in the regulations of January, 1956?

DR. DONALD CAMERON: The answers to the honorable member's questions are as follows:

1. There was no occasion for either committee to meet in 1959 or 1960.

2. Yes.

Antibiotics Conference.

MR. WHITLAM asked the Minister for Health, upon notice:

Was an Australian representative sent last year and will one be sent this year to the annual conference on antibiotics in the United States in accordance with the resolutions of the National Health and Medical Research Council in November, 1958, and May, 1959?

DR. DONALD CAMERON: The following is the answer to the honorable member's question:

There was no Australian representation at the annual conference on antibiotics in the United States last year. No representative has been appointed to attend the conference this year. The matter is under consideration.

Pharmaceutical Benefits.

MR. WHITLAM asked the Minister for Health, upon notice:

1. What rates of mark-up have been allowed since 1953 to chemists who dispense pharmaceutical benefits?

2. From what date has each rate operated?

DR. DONALD CAMERON: The following are the answers to the honorable member's questions:

1. and 2. For ready-prepared pharmaceutical benefits the mark-up has always been and still is 33⅓ per cent. or extemporaneously prepared pharmaceutical benefits the mark-up in 1953 was 50 per cent., less an overall discount of 10 per cent. In July, 1958, the overall discount was abolished making the mark-up 50 per cent.

MR. WARD asked the Minister for Health, upon notice:

1. Is there any arrangement between the Government and the manufacturing chemists and drug houses in respect of the fixing of the prices of products supplied as pharmaceutical benefits in accordance with the provisions of the *National Health Act*?

2. If so, what are the details?

3. If no such arrangement exists why was it necessary to adopt a system of price regulation in respect of retail chemists and friendly societies dispensaries but not in the case of the manufacturers and wholesalers of chemical products?

DR. DONALD CAMERON: The answers to the honorable member's questions are as follows:

1. No.

2. See 1.

3. There is no system of price regulation in respect of retail chemists and friendly societies dispensaries. There is a general agreement on prices to be paid by the Commonwealth to these bodies.

September 8, 1960.

Health and Medical Services.

MR. BLAND: I ask the Minister for Health: Has he had representations made to him from the Australian Optometrical Association alleging the existence of anomalies in the administration of the national health service? Has he considered the statement that unauthorized benefits are being paid in respect of eye treatment? If so, has he anything to say about the allegation? Furthermore, has he considered the statement that discriminatory subsidies are being made to medical benefit funds and, if so, is this a desirable feature of the system for treating eye patients?

DR. DONALD CAMERON: I am not quite sure what the honorable gentleman means by "unauthorized subsidies". There are some benefit funds which make from their own resources payments that are not matched by Commonwealth benefits. It is entirely within the jurisdiction of the funds that do make these payments to decide whether they make them or not, and the Commonwealth would interfere only if a fund was a registered fund and it was considered that its financial stability might be endangered by making them. Otherwise it is not a matter in which the Commonwealth would exercise any jurisdiction at all.

Perhaps I can answer the rest of the honorable gentleman's question by saying that the Government, since the introduction of the national health service, has steadily expanded that service in the fields of medical benefits, hospital benefits, pharmaceutical benefits, pensioner medical benefits and tuberculosis control; and, in fact, expenditure has risen from about £7,000,000 in 1950—in the early years of operation of the scheme—to an estimate of about £67,000,000 at the present time. This has been possible because of the Government's handling of the economy. It must be obvious that in the end the taxpayer must find the money for all these expansions of social welfare—and these measures are social welfare measures. They have been expanded by the Government not only in the sphere of health but in the total field of social welfare. As the honorable gentleman will be aware, my colleague, the Minister for Social Services, will introduce into this House tonight a very important measure to liberalize the means test. The Government has been able to do all these things without the imposition of heavy additional taxation to support them, and it has been able to do so because it has proceeded step by step.

Let me say this about the representations of the optometrists: The Government is perfectly aware of the great importance of the optometrical profession and of the honorable and important function it performs in the community, but if social welfare is to be expanded, it must be expanded step by step. The Government is not idle in considering any other measures that may be added to the present national health services. Unless the Government proceeds in this way, social welfare will become an incubus and not something to make the lives of citizens better. So the Government intends to proceed in the same method in the future as it has in the past, and to expand social services in accordance with the growth of the economy.

Health and Medical Services.

MR. BUCHANAN: My question, which is directed to the Minister for Health, is supplementary to the question that was asked by the honorable member for Warringah. I remind the Minister that medical fund benefits are available only to patients who have been referred to an ophthalmologist by a general practitioner. In view of the fact that optical expenses paid to any legally qualified person for testing eyes or prescribing spectacles may be claimed as a deduction for income tax purposes, will he use his influence with the fund authorities to have the present discrimination against optometrists removed, and claims in respect of spectacles prescribed by legally qualified practitioners accepted for payment.

DR. DONALD CAMERON: Perhaps I am a little dull this morning, but I cannot follow the honorable member's question. There are no medical services in which there is any Government component, but some benefit funds make payments for those services. That, as I endeavoured to explain earlier, is entirely within the discretion of the funds themselves. It would not be competent for the Government to direct the funds in this matter.

Medical Practice.

THE MEDICAL PRACTITIONERS' SUPERANNUATION FUND.

THE following are the trustees' report and the auditor's report for the year ended June 30, 1960, of the Medical Practitioners' Superannuation Fund.

Trustees' Report.

Your trustees again have pleasure in reporting satisfactory progress of the Fund during the past financial year.

The permissible scale of contributions remained unchanged as follows:

44 years of age and under	£300
Over 44 but less than 55 years	£500
55 years and over	£1000

Maximum amount of benefits not to exceed £25,000

Following a submission by your trustees, the Commissioner of Taxation has advised that doctors may join a multiplicity of funds, provided that the benefit from all sources does not exceed the foregoing figure.

In response to several inquiries your trustees have advised that a member is not prevented from continuing in membership and making contributions after he has attained the nominated retiring age (2nd proviso, clause 8 (1)).

Membership increased during the year, and contributions for the year were the highest on record and contributors' funds have shown a 50% increase since June 30, 1959.

Several members retired upon reaching the prescribed age and received their benefits from the fund, which were fully up to expectations.

Your trustees are pleased to announce an increased yield to 6% compound which has been credited to your account, a copy of which is enclosed.

Thanks are due to Dr. R. A. Lindsay for acting as delegate of Dr. O. J. Ellis (trustee) during absence overseas.

Thanks and appreciation are again extended to the Secretary and staff for continued loyalty.

The auditor's report is appended hereto for the information of members.

O. J. ELLIS,
K. JOHNS,
A. J. OSTINGA,
Trustees.

A. J. OSTINGA.
Chairman.

Report of the Auditor.

I have examined the books of account and supporting vouchers of The Medical Practitioners' Superannuation Fund for the twelve (12) months ended June 30, 1960, together with securities held as at that date.

I have obtained all the information and explanations I have required.

I have examined the balance sheet of the Fund, as at June 30, 1960, showing:

Contributors funds	£155,027	16	3
Represented by:			
Investments	145,132	9	1
Cash at Bankers	9,895	7	2
	£155,027	16	3

In my opinion, such balance sheet is properly drawn up so as to exhibit a true and correct view of the state of the affairs of the fund according to the best of my information and the explanations given to me and as shown by the books of the fund.

D. LOUDON, F.C.A.,
Chartered Accountant.

Registered under the Public Accountants Registration Act, 1945, as amended.

Newcastle,
August 17, 1960.

Royal Australasian College of Surgeons.

PRIMARY EXAMINATION FOR FELLOWSHIP.

THE following candidates satisfied the Board of Examiners at the primary examination for Fellowship of the Royal Australasian College of Surgeons held in September, 1960, and were approved: Peter Brayton Brown, John Allan Buntine, Henry Byrne, Anthony Basil George Carden, Graeme Milbourne Clark, Robin Reuben Simon Colman, David Mayo Conroy, Max Harvey Ellis, James May, Brian John Parker, Garry Eugene Scarf, Bruce Dalway Shepherd, Robert Grayson Howe Talbot, Francis Khin-Yoong Thong, Ian Herbert Wilson.

FACULTY OF ANÆSTHETISTS.

Primary Examination for Fellowship.

THE following candidates satisfied the Board of Examiners at the primary examination for Fellowship of the Faculty of Anæsthetists of the Royal Australasian College of Surgeons held in September, 1960, and were approved: Maxwell John Kirwan, Thomas Leonard O'Connell, John Joseph O'Leary, Agnes Esther Sinclair.

Notes and News.

Nuffield Foundation.

Grants for Research Projects in Australia.

The Chairman of the Australian Advisory Committee of the Nuffield Foundation, Mr. Colin Syme, announces that the Foundation has continued its support of Australian research by making available £75,000 over a period of five years for research projects of outstanding merit and interest.

One of the Foundation's main activities in Australia is the support of research programmes which are concerned with specifically Australian topics, or for whose development special facilities exist in Australia. In the past, support has as a result been largely directed to the biological and anthropological fields, but the Foundation does not necessarily wish to confine its activities to these fields, and any type of scholarly project with an Australian flavour will be considered.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED SEPTEMBER 3, 1960.[1]

Disease.	New South Wales.	Victoria.[2]	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.[2]
Acute Rheumatism	1	..	5(2)	..	..	..	..	..	6
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	3	..	..	..	..	..	4	..	7
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	6(1)	..	7(4)	2(1)	2	..	2	2	21
Diphtheria	..	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	..	..	1	1(1)	..	..	..	3	5
Encephalitis	..	..	..	..	..	..	..	..	..
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	98(41)	..	12	18(6)	3(2)	1	..	3	135
Lead Poisoning	..	..	3(3)	..	..	..	..	..	3
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	5	..	..	..	..	..	5
Malaria	..	..	2(1)	..	..	..	1	1	4
Meningococcal Infection	1	..	..	..	..	..	..	..	1
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	1	..	..	..	..	..	..	..	1
Puerperal Fever	..	..	1	1	..	..	..	..	2
Rubella	..	..	..	..	..	..	..	1	1
Salmonella Infection	..	..	..	1(1)	..	..	..	..	1
Scarlet Fever	14(10)	..	..	4	2(1)	1	..	1	22
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	..	..	5	..	5
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	21(11)	..	4(1)	3(1)	8(4)	2(1)	6	..	44
Typhoid Fever	..	..	..	..	..	..	1	..	1
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

[2] Figures incomplete owing to absence of returns from Victoria.

The Australian Advisory Committee is able to accept applications for research grants at any time. In general, projects submitted for consideration must be of particular merit and interest or show particular promise, and they should be of a kind which can be well done in Australia. The Foundation is not inclined to support projects for which support from other sources should be available; nor, except in special circumstances, will it provide subsidiary support for a project sponsored primarily by another organization. Requests for the provision of equipment are likely to be granted only if they are incidental to a research project which the Foundation feels able to support.

Support for a given project may be provided for any period up to five years subject to review by the Committee whenever this seems called for. When the work results in material *of high quality not readily published through normal channels*, the Foundation will consider making a grant towards the expenses of publication.

Applications for grants should be addressed to Mr. N. H. Oliver, Secretary, Nuffield Foundation Australian Advisory Committee, Engineering Chemistry Laboratory, University of Melbourne, Parkville, Victoria.

Grants for Visitors.

From time to time the Foundation is willing to sponsor the visit of an academic leader to Australia from Britain or another country of the Commonwealth. It is expected that any such visit should be primarily to allow Australian workers in a particular field of scholarship to benefit from contact with a person who is doing outstanding work in that field. It should involve extended departmental and laboratory visits and discussions, or some specific research activity in Australia. Support for visits solely to attend specific conferences or consisting simply of a programme of lectures will not normally be considered.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Conference at Cooma.

THE Post-Graduate Committee in Medicine in the University of Sydney, in conjunction with the Far South Coast and Tablelands Medical Association, will hold a post-graduate conference at Cooma District Hospital on Saturday and Sunday, November 12 and 13, 1960. The programme is as follows:

Saturday, November 12: 2 p.m., registration; 2.15 p.m., "Alcohol and the Law", Dr. John McGeorge; 3.45 p.m., "Management of Head Injury", Dr. S. M. Morson.

Sunday, November 13: 9.30 a.m., "Thyroid Disease", Dr. A. E. McGuinness; 11 a.m., "Psychiatry in General Practice", Dr. John McGeorge; 12 noon, "Lumbar and Cervical Disc Lesions", Dr. S. M. Morson; 2.30 p.m., "Diabetes", Dr. A. E. McGuinness.

The fee for attendance at the course is £3 3s., and those wishing to attend are asked to notify Dr. G. H. M. Wallace, Honorary Secretary, Far South Coast and Tablelands Medical Association, Massie Street, Cooma, as soon as possible. Telephone: Cooma 307.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Walsh, Thomas, M.B., B.Ch., 1950 (N.U. Irel.), 45 Hinkler Crescent, Lane Cove.

Stewart, Frederick Harold, M.B., B.S., 1959 (Univ. Sydney), 221A Burwood Road, Burwood.

Shearer, Alex Michael, M.B., B.S., 1959 (Univ. Sydney), 160 Bland Street, Haberfield.

Deaths.

THE following death has been announced:

GOLDSWORTHY.—Neil Ernest Goldsworthy, on September 26, 1960, at West Pymble, N.S.W.

Diary for the Month.

OCTOBER 11.—New South Wales Branch, B.M.A.: Executive and Finance Committee; Organization and Science Committee.
OCTOBER 13.—New South Wales Branch, B.M.A.: Public Relations Committee.
OCTOBER 14.—Queensland Branch, B.M.A.: Council Meeting.
OCTOBER 17.—Victorian Branch, B.M.A.: Finance Sub-Committee.
OCTOBER 18.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

Authors of papers are asked to state for inclusion in the title their principal qualifications as well as their relevant appointment and/or the unit, hospital or department from which the paper comes.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

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